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Senator Claude Pepper who introduced the Neeley-Pepper Bill, S. 93, into the 80th Congress on January 8. The Neeley-Pepper Bill, which calls for a $100,000,000 Federal expenditure for cancer research, failed to pass the 79th Congress.

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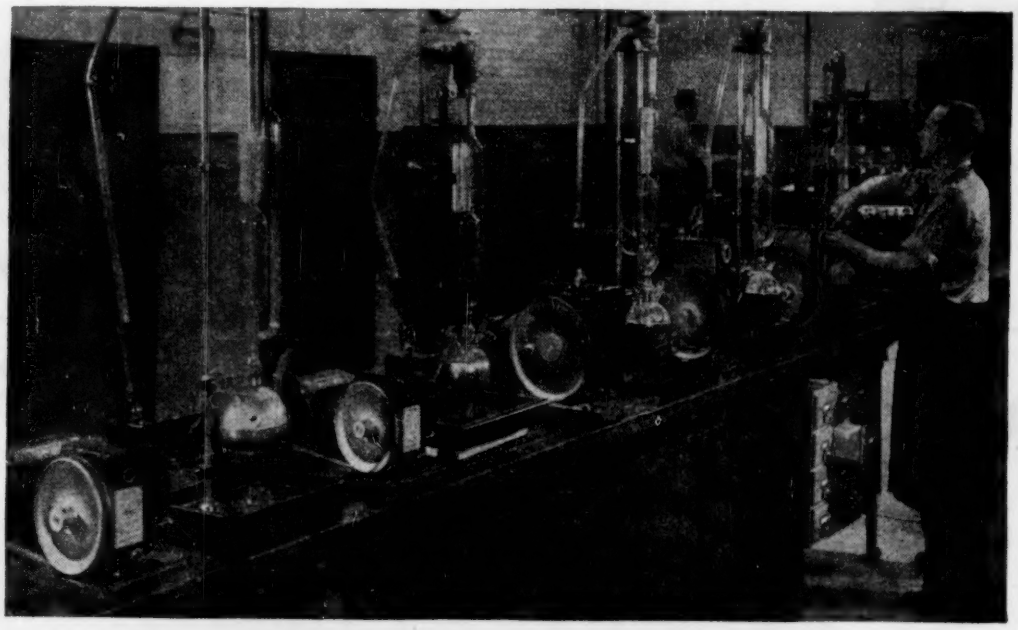
Financing Cancer Research

E. V. Gowdry

Welch

DUO –  – SEAL

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Science

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Financing Cancer Research

E. V. Cowdry

Washington University, St. Louis, and *Barnard Free Skin and Cancer Hospital*

FAILURE OF THE NEELY-PEPPER BILL, calling for an appropriation of $100,000,000 for cancer research, to pass on July 27, 1946 was not the reflection in Congress of any unwillingness on the part of the public to foot the bill. On the contrary, the results of a Gallup Poll, reported on June 12, indicated that 87 per cent of voters were ready to support the Neely-Pepper program and that 72 per cent were even willing to pay extra taxes to provide the money. The bill failed because the experts could not pull together and advise our senators and representatives as to just what is needed. A similar confusion of tongues led to failure of legislation designed to foster scientific research by the establishment and maintenance of a National Science Foundation.

We must profit now by experience and frame a new cancer bill which will pass unanimously. First, it is essential to show, to the satisfaction of cancer experts, how $100,000,000 can be advantageously spent on cancer research with the single purpose of overcoming this disease as quickly as possible. Second, it is equally essential to show, to the satisfaction of Congress, how expenditure of this sum can be properly controlled.

Six objectives are worthy of consideration:

(1) *To expand cancer research facilities throughout the United States.*

At present most of the work is concentrated in the great cities along the Atlantic Seaboard. Except in the state of Missouri, there are no cancer hospitals west of the Mississippi which are recognized by the American College of Surgeons. In a general way the *age-adjusted* death rates from cancer per 100,000 population of the several states are indices of the alertness of the medical profession in the recognition of cancer, not of its actual frequency. According to data published in April 1946 by the National Cancer Institute, the two highest rates are those of New York and Rhode Island, with 144.61 and 138.43 per 100,000; the two lowest are those of Arkansas and New Mexico, with 62.25 and 71.13, respectively. Evidence such as this strongly suggests that citizens in the western and southern states have not an equal chance for cancer diagnosis with those in the eastern ones. California stands out in the Far West with the high rate of 118.43. In the testimony at hearings of the Neely-Pepper Bill the Midwest and Far West were inadequately represented; of a total of 24, only 3 persons from west of the Mississippi were heard, compared with 11 from New York City.

The outstanding cancer research centers of the world are the National Cancer Institute near Washington, D. C., operated by the Government (U. S. Public Health Service), and the Memorial Hospital in New York. They seem a long way off to westerners, some of whom are getting weary of voluntarily contributing fairly large sums, much of which is sent to New York and is expended mostly in the East. It is not surprising that they welcome a proposal that has been presented to the National Advisory Cancer Council of the U. S. Public Health Service, and by Dr. Sherwood Moore in testimony at a hearing of the Neely-Pepper Bill, in accordance with which pilot cancer centers, on a par with the National Cancer Institute and the Memorial Hospital, would be established and maintained in the Middle and Far West. The one for the Middle West should be an expansion of the Barnard Hospital in St. Louis, which for long years has been a pioneer comparable in a small way with Memorial Hospital in New York. St. Louis is a more strategic location than Chicago for this purpose, because the states immediately west and southwest of it are less adequately provided with cancer facilities than Iowa, Wisconsin, and Minnesota, west and northwest of Chicago. St. Louis stands on the border of a very large territory, commercially tributary to it, in which the influence of such a Midwest Center would lead to the development of cancer facilities still more conveniently located. San Francisco is probably better located than Los Angeles for the Far West, or Pacific Cancer Center.

Construction and equipment of each of these strategic centers would cost about $5,000,000. In addition, some expansion of cancer facilities in the East and throughout the United States is urgently needed. The total cost of necessary enlargement of such facilities can be conservatively estimated at about $20,000,000. Since there is urgency in this need for working space for both laboratory and clinical research, high priority should be given to construction of buildings and purchase of equipment.

(2) *To increase the effectiveness of cancer investigators without waiting to train them.*

These individuals are in three categories: (a) Expert clinicians, now busily engaged in treating cancer and patients suffering from other diseases, should be enabled to devote all their energy and skill to the cancer patients. If this could be arranged, it might further be feasible to encourage these clinicians constructively to attack aspects of the cancer problem that can be solved only in the clinic, even in some cases to take time off from practice for this purpose. They cheerfully rallied to the Nation's call in the war. Many of them will be no less ready to attack cancer in times of peace. (b) Persons now working only part time on cancer research should

be persuaded to devote full time to such research. I have in mind staff members of universities and medical schools who have proved themselves as productive cancer investigators in the time that they have been able to spare from their other duties. To get at the facts, a survey should be made of these individuals. This would probably show that a large amount of excellent work is at present being done by them, and that this could easily be doubled or trebled if they were to devote all their time and energy to the task. (c) Cancer is a problem peculiar in the fact that so many types of training can be utilized in its solution. Numerous physicists, biochemists, physiologists, pharmacologists, and others, by virtue of experience already mature, are well fitted without delay to play leading roles in this kind of research. Carefully selected individuals in this category might easily be induced to devote a year, or several years, to this inspiring task.

A new attitude toward these and other cancer investigators must prevail. They should not be expected to labor merely for the love of it at the smallest salary they will accept, but should be paid high salaries all along the line. We have witnessed key men in government, who worked for the country during the war at minute salaries, one after another seek employment now that the war emergency is over. Cancer is a very real threat to all of us, and the best brains of the Nation must be harnessed regardless of cost. To be content with second-raters would be to jeopardize the whole campaign against cancer. Yet this will be exactly the tendency of the more conservative of the cancer experts, who will say that so-and-so is best qualified but is beyond our reach.

(3) *To make sustaining grants for cancer research.*

Increases in facilities and personnel are not justified except for investigations that can be organized and sustained over a considerable period. Those of us in the field have often had to content ourselves with annual grants. A lot of good work has been financed in this way, and not infrequently the grants are repeated year after year. But, since there is usually no guarantee of continuing financial support, in all fairness one has to warn prospective members of his staff that they may soon have to seek other jobs. No one would blame a young man, beginning a career of promise, if he chose, instead, an appointment with more security. Older workers, who have proved themselves and have fairly secure positions, are naturally not attracted. In case a young man does gamble with his future and, by virtue of the success of his cancer research, is continued for 10 years or more by a succession of annual grants, he will then find himself with no accumulating annuity payments against eventual retirement, because this measure of protection is never provided in grants for cancer research. Being still young, he may say that he does not care, but we know that he will care later. A reasonable degree of economic security must be given cancer workers, not only in attractive continuing salaries, but also in some effective system of annuity—for instance, 10 per cent of salary paid into the annuity fund by the employer and 5 per cent by the employee.

Obviously, the largest item in the expenditure should be in the nature of sustaining grants for salaries, annuity payments, and operating expenses. These should be made to nonprofit institutions of recognized standing coincident with the above-outlined increases in plant and personnel. The said institutions should be required to invest these sustaining grants in Federal bonds. In size, the grants should be sufficient to carry the projects for 20 years, the recipient institutions expending interest and cashing bonds. This policy would amount to Federal endowment of cancer research. The amount of the expenditure should be about $60,000,000.

Precedent for Federal endowment of research in public institutions is found in the Purnell Act "to authorize the more complete endowment of Agricultural Experiment Stations" (see *Budget of the U. S.*, 1945, p. 230). Unless the policy can be adopted of aiding private institutions on a par with public ones, the idea of bringing all our institutional strength to bear on the cancer problem will be an idle dream. The Department of Agriculture is activated by a pressure group, the farmers of the Nation, and it has achieved wonders. The $60,000,000 to stabilize and maintain certain projects in cancer research on a sound basis for 20 years looks small in comparison with the Agricultural Research Administration general account of $40,313,650 in 1944 and $47,123,140 in 1945—not to mention additional millions for special investigations. We now have a group, known as the "Sponsors of Government Action Against Cancer," which is pressing for action and will not accept "no" for an answer. It is to be expected that within a few years other researches on cancer will similarly require stabilization and that this will be one of the accomplishments of the next $100,000,000 appropriation, with which we are not now concerned.

(4) *To produce special supplies and equipment.*

It frequently happens that cancer research is held up for want of certain chemicals that are hard to obtain. Some of them have to be made for the purpose. Physical apparatus is often required which is not on the market and which manufacturers will not take the trouble to design and produce, because it would not be high priced and would never be wanted in quantity. The best way to remove these obstacles that cause most annoying delay and inhibit research would be to establish and maintain a Central Physiochemical Institute for supplies. Such an organization would help not only by giving advice as to feasibility of implementing the ideas of cancer workers, but also by manufacture and, perhaps, by loaning costly apparatus which is available and the need for which might be only temporary. Moreover, reliance on service

by the Institute would be economical, for it would relieve research organizations of the necessity of having their own usually poorly equipped mechanical shops and synthetic chemical laboratories. The Institute might well act as a clearinghouse for distribution of isotopes which are now of such importance. Cost to build and equip the Institute might be in the neighborhood of $2,000,000 plus operating expenses of, say, $500,000 a year for 20 years, making a total of $12,000,000.

(5) *To focus cancer research on the human problem.*

The Committee on Growth of the National Research Council, financed by the American Cancer Society, is wisely approaching the cancer problem on a very broad basis. Anything having to do with growth, even remotely, is included as cancer research because of the bearing it may have on malignant growth. All kinds of living things from plants to man are included, because observations on all forms of life may well afford clues to conditions in man. Very few of the 95 grants made by the Committee through June 15, 1946 and amounting to a total of $623,057 related to cancer of definite types in specified organs or tissues. Several concerned breast cancer in mice; two, leukemia; one, melanoma; one, cancer of the thyroid; two, the Brown-Pearce tumor of rabbits; one, normal and malignant fibroblasts; one, the rabbit papilloma virus; and one, leukemia, Hodgkin's disease, etc. Research specified as dealing with cancer of the uterus, stomach, lungs, and other organs of the body was not included. Yet the basic investigations promoted by the Committee on Growth are all to the good. They should be supported from the proposed $100,000,000 appropriation if the funds collected by the American Cancer Society prove insufficient, and other equally fundamental researches should be initiated.

To supplement this fine general and fundamental program of the Committee by developing a different line of attack, it is proposed, with part of the Federal appropriation, to focus research on specific cancers in man. The physician has to diagnose and treat cancer of the stomach, uterus, skin, brain, lungs, and so on through all parts of the body. Cancer in all locations has some features in common, on which light may be expected from the basic researches referred to; but cancer in each of them must be considered individually because of individual differences in the operation of certain important factors. Thus, exposure to external influences like sunlight, which, in excess, is known to cause cancer, is greatest for the skin and negligible for the brain. Mechanical injury is of consequence in cancer of the breast, testicles, bone, and skin and insignificant with respect to the appearance of cancer of the pancreas and lungs. Conditions of cell life in the several parts of the body are of acknowledged importance in regard to the malignant transformation. Since these conditions are far from uniform, they cannot be ignored but must be purposefully taken into consideration. Some tissues have an abundant blood supply, while others are avascular; some are more under the grip of internal secretions than are others, and the functions performed by each are related to needs for supply and removal of waste. Another consequence of the different functional roles is that the symptoms of early cancer will, to some extent, be dependent on the particular function disturbed by the cancer. Therefore, we have to attack cancer wherever we find it, marshaling all available knowledge of specific conditions in every part.

The system of panels advocated would be specifically for uterine, skin, gastric, and lung cancer, and so on down the list of some 20 or more. Each would have a chairman and a vice-chairman, both usually clinicians and, when feasible, of rather different views and training. For instance, the hematologists heading the panel on leukemia (blood cancer) could well represent quite divergent schools of thought. Also, it would not be difficult to find two leading gynecologists for the panel on uterine cancer who would bring different and supplementary experience to bear on the problem. Two leading dermatologists for the panel on skin cancer would supply more effective coverage than one. The other members of each panel should include a physiologist, a biochemist, a pharmacologist, a radiologist, a cytopathologist, an endocrinologist, a nutritionist, a geneticist, and possibly others, each one particularly qualified by experience to deal with problems of the panel. It would be essential for a considerable number of these other members to be engaged in the experimental study of cancer in the organ represented by the panel. The membership of panels should gradually change to bring in the best talent from the whole Nation.

The defeatist will question the usefulness of such panels, saying that there is no assurance that progress will result from these direct attacks and even implying that, in his judgment, the only worth-while strategy is to concentrate on fundamentals—a nice comforting term—and for the time being to ignore special cases. We agree, as already stated, that work on fundamentals must be not only continued but extended with the aid of the $100,000,000 appropriation. In addition, however, we plead for consideration of the cancers in the very regions of the body where they are death dealing. There is reason to hope for significant advances by some of these panels. Reports to the Nation of no progress with respect to types of cancer from which citizens are dying by the thousands would increase determination to make progress. It is not beyond the bounds of possibility that means may be discovered satisfactorily to treat cancer before we learn all the secrets of its nature. In fact, a specific treatment for the greatest human killer in view of number of deaths—malaria—was discovered before the cause was determined. Means of prevention of scurvy was discovered long before its nature was revealed. Several similar examples can be cited. In

my opinion, these regional cancer panels are justified as one major part of the grand strategy of the campaign.

The panels should meet regularly four times a year, twice in the East, once in the Middle West, and once in the Pacific states, a limited number of nonmembers in each region being invited to attend and present their work. This, like the strategic pilot centers, would tend to draw all parts of the country into the effort. At one meeting each year leading cancer investigators from abroad should cooperate. Yearly digests of world literature on cancer in the domain of each panel, together with the most up-to-date possible accounts of prevention, diagnosis, and treatment and a summary of research in progress, should be published and widely circulated.

The cost of this regional panel system is difficult to estimate, but the item for travel would be substantial. It is further proposed to make each participant a per-diem payment, as with medical consultants to the Veterans Administration, and, naturally, to cover cost of a full-time secretary for the chairman of each panel, printing, postage, etc. It might amount to $200,000 a year, or, for 20 years, $4,000,000.

(6) *To promote international cooperation in the war against cancer.*

Clearly, cancer is a world problem, and we, ourselves, can have no monopoly of wisdom. It would be highly desirable to arrange for distinguished foreign cancer specialists to come and work in our laboratories for a year or more. Particular types of cancer research in this country will be benefited, and their own experiments at home will also be advanced thereby. Also, carefully selected American cancer investigators should work in foreign countries under the same proviso of mutual advantage. They should be given not merely travel expenses but an allowance for scientific expenses of their work abroad so that they would not constitute a financial burden on the host institutions. A special American committee, working through the newly formed World Health Organization (*Science*, September 27), should be charged with promotion of this international cooperation, with ability to draw on an appropriation for this purpose of $3,000,000.

Control of Expenditure

It is a waste of time to suggest any plan for delegating administrative control to any private agency, since Congress will insist on Federal control of Federal expenditures. Within the Federal Government it is obvious that the U. S. Public Health Service is best fitted to act in this capacity. A division of the Service, the National Cancer Institute, with its advisory body of the Nation's outstanding cancer experts, the National Advisory Cancer Council, has been recommending grants for cancer research to both public and private institutions for nearly 10 years under authority of the National Cancer Institute Act. All that is necessary is to strengthen this Council so that it will be able to discharge the greatly increased duties contemplated in the proposed new cancer bill. This can probably be accomplished without any change in organization or operation which would be considered controversial.

The officers of the Council should continue to serve in their present capacities: the Surgeon General of the U. S. Public Health Service as *chairman*, ex officio; the chief of the National Cancer Institute of the U. S. Public Health Service as *secretary*, ex officio; and the *executive director* as an appointed official.

The other members of the Council should be increased in number to nine, and the policy should be adopted of making them still more representative of the whole Nation. This could be accomplished in several ways. Rotation of membership has proved satisfactory. With the increase in number, and with period of service three years, three members should be replaced annually by new appointees recommended by the Council. In order regularly to draw "new blood" into the Council, retiring members should not enjoy the privilege of subsequent reappointment, but the active interest and advice of these retiring members should be retained by appointing them members emeriti of the National Advisory Cancer Council. It is proposed that they should meet regularly once a year in the National Cancer Institute and that matters of consequence should be submitted to them for advice on this occasion and also informally at other times.

Another means of making those engaged in cancer research throughout the land feel that the Council is theirs hinges on both membership and meetings. At present, cancer research is mainly centered in the eastern states. Since it is clearly desirable to encourage people in other parts of the country, also possessed of great resources, to engage in the war on cancer with all their might, it would be a wise policy to begin by recruiting members of the Council from west of the Mississippi in the ratio of one to every three from east of the Mississippi. This would amount to a substantial increase in western representation. By the same token, regular meetings of the Council every two months should be held west of the Mississippi in the same ratio of one to every three east of the Mississippi.

The members of the Council not only should be increased in number but also should be enabled to devote more of their time and energy to this service which can mean so much to the people of the United States and to all lands. Though willing and eager to serve without recompense, each of the 12 members of the Council should receive a yearly salary of $5,000 in addition to travel expenses. Moreover, failure from whatever cause to attend two consecutive regular meetings of the Council should be construed as resignation from membership. To operate effectively the Council would require adequate full-time assistance of experts, but the

total administrative cost should not exceed 1 per cent of the whole appropriation, namely, $1,000,000.

It is essential that the Council have power to recommend grants for construction of cancer facilities and for expenses of research over periods not to exceed 20 years. Expenditure of all grants by recipient institutions should be audited in accordance with the usual procedure of the U. S. Public Health Service. In selecting projects to be aided, the Council should have complete discretion. The expenditures outlined earlier are, of course, merely suggestions to indicate that $100,000,000 is needed for disbursement in the first 5 years. More will probably be required, and the administrative machinery outlined is intended to carry on for 20 years with the aid of subsequent appropriations establishing other lines of cancer research on an equally firm financial basis.

It would save time and avoid confusion and embarrassment if the Council were to take the initiative—that is, not merely to wait for the shower of high-pressure applications certain to be received if such a cancer bill is passed by Congress but, instead, actively to investigate needs and to invite and assist cancer research institutions considered worthy to formulate projects. No applications for financial aid not originally solicited by the Council should be accepted.

There is a chance that a bill along these lines would go down in history as marking a new era in human welfare in which all-out financial support is provided by government, not for war or for any commercial advantage, but to solve a definite problem in medicine. It is fitting that cancer should be the first disease so attacked. The public is of one mind in this matter. If the experts raise their sights and organize research with skill and wisdom on a large scale, and the policy is adopted of subsidy of long-term projects wherever it is most advantageous throughout the United States, the results will justify many times this expenditure, and the precedent will have been set for a similar approach to other devastating human diseases. Indeed, such a bill would signalize a new kind of emancipation—one of freeing the people from what is believed to be needless suffering and from untimely death.

Scientific Development of the Use of Human Resources:

Progress in the Army Air Forces

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THERE ARE FEW WHO WOULD QUESTION the fact that by far the most important of the resources available to us are human talents. It is also true that there are few areas in which so little progress has been made in the observation and classification of facts and the establishment of verifiable general laws as in the study of human resources and their utilization. This paper will attempt to show that a science can be developed regarding the use of human resources. Some of the recent findings resulting from the increased activity during the war years will be presented primarily to illustrate the types of research and experimentation which can be expected to be productive of results of practical significance.

The general field in which further research and experimentation is proposed includes the more accurate description of the individual in terms of his aptitudes, basic interests, temperament, and potentialities; the training and education of this individual with such methods and materials as to enable him to make maximum use of his personal endowment; his guidance into the types of vocational and avocational activities which will be of greatest assistance to him in his further development; and evaluation of his success in the activities in which he participates.

In this field certain laws and principles were established by psychologists a number of years back. These relate especially to such matters as learning, forgetting, perception, and motivation. More recently, individual differences and trait differences and their implications for participation in various types of activities have been the subjects of extensive investigation. Scientific research on these matters requires very large groups of individuals, and some of the problems also necessitate waiting several years before final evaluation can be made. In most situations the extent of control of the individuals taking part in an experiment is also quite limited.

In many respects the military situation during wartime is ideal for this type of research. Large numbers are readily available. The life cycle from the time of individual analysis and classification, through training, and on to performing the job for which the individual was selected and trained is compressed into a period of only two or three years. Furthermore, the necessities of war give military authorities a much greater degree of control of the individual with public approval than would ordinarily be possible.

Having the resources of this large laboratory to work with, including the availability, for the staff, of a large

Presented at the Annual Meeting of the National Academy of Sciences, April 22, 1946.

number of the best psychologists in the country, it has been possible to make important contributions to this branch of scientific knowledge in spite of the pressure to obtain immediately useful practical results in the military situation.

One of the most fundamental tests of the value of a body of knowledge including relationships is the ability to predict events on the basis of information already available. In working with human beings it is much more difficult to obtain full knowledge of all of the large number of relevant factors. In practical situations it is usually desirable to predict from a few relevant items known to represent an oversimplification and only partial coverage. Under these circumstances, the predictions must necessarily be in terms of probabilities which are far less than perfect. Such predictions, however, may be of very great value in certain practical situations.

The higher the pilot stanine, the greater the chances of success in primary pilot training

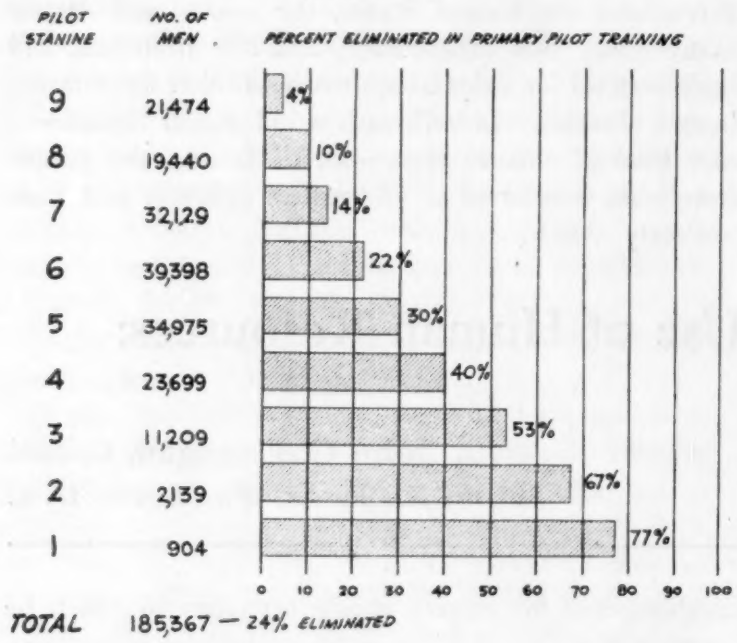

FIG. 1. The bars indicate the proportions eliminated at each pilot stanine. Elimination was for flying deficiency, fear, and own request. Flying experience credit is included in the stanine score. The data are from classes 43-F through 45-H. Men with low stanine scores are now disqualified for training; most of the men with low stanines included in the chart entered primary schools early in 1943.

The original research problem assigned to psychologists in the AAF for scientific investigation early in the period of the recent national emergency was to predict, on the basis of an evaluation of individuals before they begin flying training, which of them would later prove to be the most successful as airplane pilots. As the result of an initial analysis of the requirements of the job and a continuous program of research and follow-up, it was possible to assign weighted aptitude scores ranging from 1 to 9, for the designation of which the term *stanines* (standard nines) was coined. These were based on a battery of 6 apparatus tests of coordination and speed of decision and 14 printed tests including intellectual aptitudes and abilities, perception and visualization, and temperament and motivation. The weighted aptitude scores obtained from these tests were of great value in the selection and classification of applicants for pilot training throughout the recent war period.

Fig. 1 shows the experience during the war in the follow-up in primary pilot training schools of 185,000 men assigned these scores. It will be noted that of the more than 20,000 men obtaining the highest stanine (9) only 4 per cent were eliminated from training. Men obtaining lower stanines had progressively larger proportions eliminated, right on down to the group of about 1,000 men with the lowest stanine (1), 77 per cent of whom were eliminated in primary flying training.

Men with low pilot aptitude scores (stanines) on the AAF aircrew classification tests are very poor prospects for pilot training

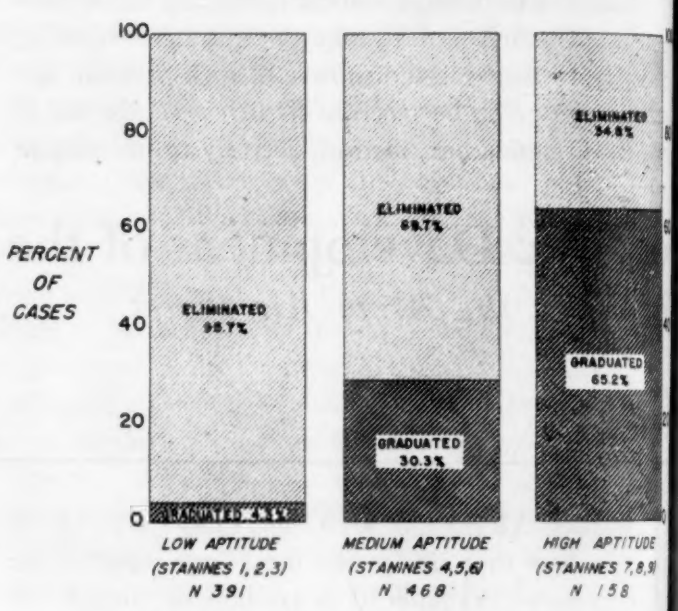

FIG. 2. Results for the experimental group.

Qualifying standards in terms of stanine scores were raised successively until, in the fall of 1944, only men with stanines of 7, 8, and 9 were admitted to pilot training. This improvement in the aptitude level of those sent into flying training made possible the raising of training standards and also resulted in the requirement of a higher degree of flying skill and general proficiency for graduation from flying schools.

In order to provide a comprehensive evaluation of the selection procedures under the new training conditions an experiment was initiated in the summer of 1943. A sample of more than 1,000 men was selected by representative AAF Examining Boards throughout the country. All of the usual tests of aptitude, ability, temperament, and coordination were given to this group, but regardless of their scores on these tests, all those who met the physical standards of the medical examination were accepted and sent into pilot training. The scores for the various aptitude tests were combined according to current procedures, and the men were assigned the usual stanine scores for pilot aptitude. However, the records were sent directly to Headquarters of the AA

Training Command, and no indication as to whether the man had obtained a high or low stanine was made available to the training schools.

The results of this experiment are shown in Fig. 2. Members of the experimental group were scattered in various schools and received their flying training in classes graduating in 1944 and 1945. Only 4 per cent of the men with low aptitude (stanine of 1, 2, or 3) were able to complete the full course of flying training. The remaining 96 per cent were eliminated at some stage of their training. Not one of the 125 men with the lowest aptitude score (1) was successful in flying training. Of

The pilot stanine was effective in predicting success in pilot training for West Point Cadets

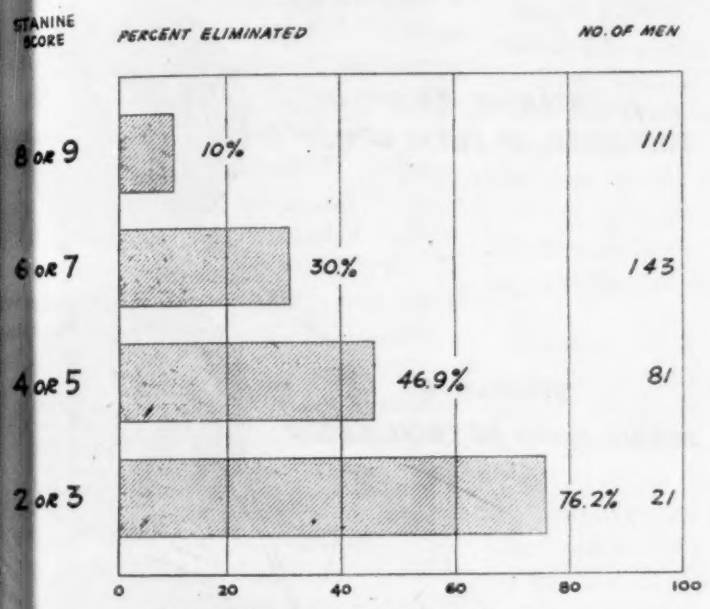

FIG. 3. Results for West Point Cadets.

the men with medium aptitude, 30 per cent were graduated. The men with stanines of 7, 8, and 9, which has been the qualifying standard since the fall of 1944, had a graduation rate of 65 per cent under the new standards in effect in flying training classes in 1944 and 1945. It is clear from these data that very important improvements in training efficiency resulted from the use of these objective selection procedures.

To check these findings with a group which had been carefully selected, but on other bases than pilot aptitude, an experimental study was made of the class of 1946 at the U. S. Military Academy at West Point. Here again, as shown in Fig. 3, the pilot stanine predicted success in flying training. Only 10 per cent of the 8's and 9's were eliminated, while almost half of the 4's and 5's and more than three-fourths of the small number of cadets whose scores placed them in the lowest group (those with 2's and 3's) were eliminated in primary flying training.

Follow-ups in regard to accident rates, success in transitioning to combat-type planes, and selection as airplane commanders rather than copilots confirm the predictive value of the pilot stanine. For example, 50 per cent more of the fighter pilots receiving combat training in the First Air Force with pilot stanines of 7, 8, and 9 scored in the top half of the class in hits on aerial and ground targets than did men with pilot stanines of 5 and below (see Fig. 4).

The initial emphasis in the psychological research program in the AAF was on pilot *selection*. However, this emphasis shifted rapidly in the practical situation to one of *classification*. Superior pilots are not of great value for bombing operations unless they are accompanied by superior navigators, bombardiers, flight engineers, radar observers, and gunners. Fortunately, it was found that the aptitudes and traits most important for each type of duty differ in various respects, so that by making an accurate analysis of each individual's potentialities in

High stanine pilots were likely to score more hits on aerial and ground targets

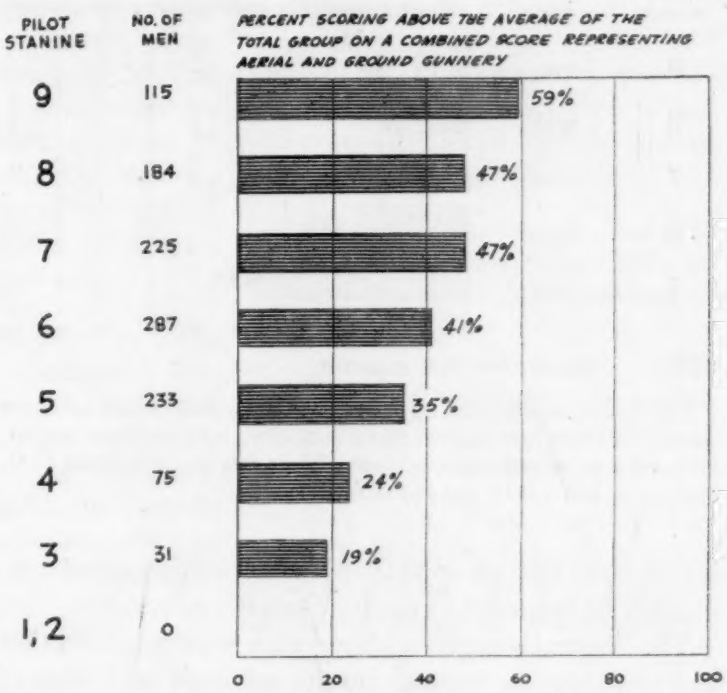

FIG. 4. Data collected from stations and commitments in the 1st Fighter Command between June 1944 and March 1945. Only newly rated pilots are included.

relation to the requirements of the various jobs, it is possible to improve the quality of the personnel available for all positions.

This is illustrated in Fig. 5, which shows the relation of the navigator aptitude score to success in navigation training for approximately 15,500 men. The men with navigator stanines of 8 and 9 were remarkably successful, with only 8 per cent and 3 per cent, respectively, failing to graduate. It is of great importance to the general problem of the use of human resources to note that most of these men had *pilot* stanines of only 6 and 7, and many of them were as low as 3, 4, and 5.

For bombardiers there was, in addition to the usual training school studies, an opportunity to follow up the actual combat results of these men in terms of the distance their bombs fell from the assigned enemy target. The radial or circular errors of 1,300 bombardiers were obtained from photographs taken at the moment of impact of the bombs and compared with the bombardier aptitude scores achieved by these men when they took the Aircrew Classification Tests prior to training, ap-

proximately two years earlier. These results are shown in Fig. 6. Although the differences are small, when it is remembered that combat conditions are far from standardized and many factors such as the skill of other members of the crew, weather conditions, the strength of enemy opposition, and the condition of the plane's equipment tend to attenuate the relations observed, the finding of a difference of 100 feet in the average accuracy of bombardiers with bombardier stanines of 7, 8, and 9, as contrasted with those with bombardier stanines of 5 and below, is of great practical significance. The group

The higher the navigator stanine, the greater the chance of success in advanced navigator training

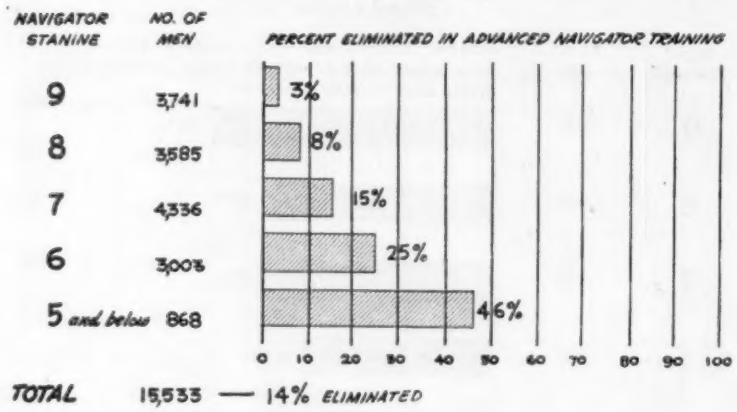

FIG. 5. The bars indicate the proportions eliminated at each navigator stanine. Elimination was for flying deficiency, fear, and own request. Only new aviation cadets are included. These data are from classes 43-12, 43-13, 43-14, 43-17, 43-18, and 44-1 through 45-13.

is also large enough so that this relationship cannot reasonably be regarded as due to chance.

The illustrations given above with regard to selection and classification indicate results achieved with respect to one aspect of the work of the Aviation Psychology Program. Similar results were achieved in the improvement of certain aspects of training and in the evaluation of success by applying the same scientific methods to problems in these areas.

In developing the battery of tests, the general procedure was to make a systematic survey and exploration of the requirements for success in the activity. This requires knowledge of basic psychological traits and professional insight and skill in translating the apparently critical requirements for success into testable hypotheses in the form of examining procedures. Experience in the AAF indicates that the most productive procedures for developing tests which will have predictive value involve the standardization of the test situation so that the individual knows exactly what his task is and how failure on specific parts of it will affect his score. It must be possible to make the task very nearly identical for all individuals. This means that, if apparatus tests are used, they must be accurately calibrated to insure comparability of difficulty. Although much ingenuity and judgment is required in setting up the sample of performance which is to constitute the test, the scoring should be as objective and free from the subjective judgment of the scorer as possible. The final result should be expressed in one or more simple numerical scores. Such scores are clearly abstractions and oversimplifications, but they represent data which can be evaluated.

Such tests representing hypotheses regarding the essential elements of a practical situation must be evaluated. The validity or predictive value in specific situations can be easily determined if a measure of success in the activity can be obtained. On the basis of such follow-up data the test can be revised, and the whole process of

Lead bombardiers with high bombardier stanine tend to have lower average circular errors

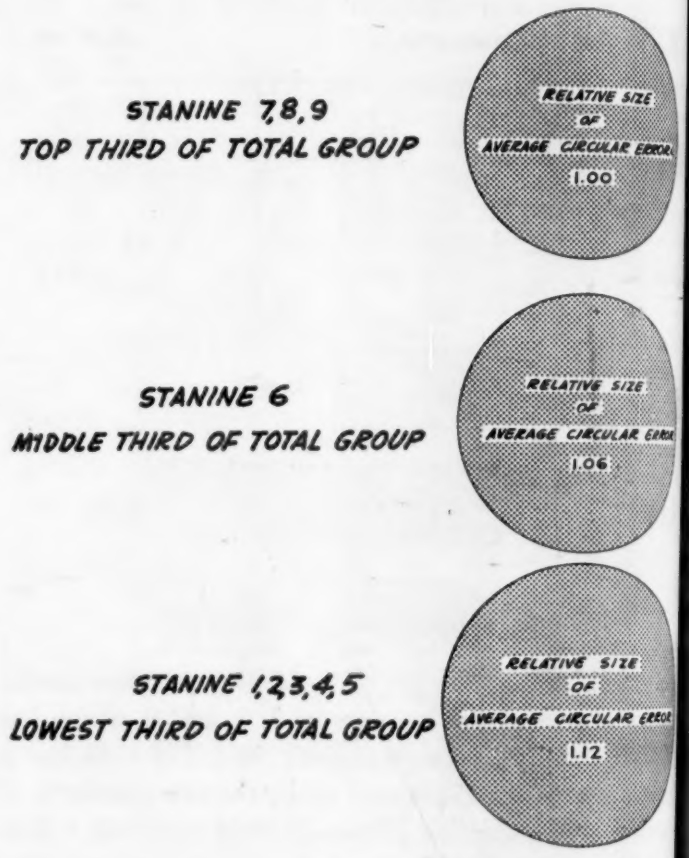

FIG. 6. These figures represent a composite of all of the data collected from the 8th and 15th Air Forces on the relation between circular bombing error and the bombardier stanine.

exploration, hypothesis, experiment, and evaluation repeated in the light of the new findings.

It is believed that the results of the past few years have demonstrated that the application of scientific methods to problems of human resources and their utilization can be of great practical value. Progress has been delayed in the development of this field of knowledge because of the need for large experimental groups, long periods of time, and substantial resources. However, the possible benefits are of great importance from the standpoint both of the general welfare and progress of the country and of the human values involved. It is therefore essential that strong support be given to a coordinated scientific research program on the use of human resources.

NEWS *and Notes*

An additional announcement from AAAS Council through F. R. Moulton, administrative secretary, names the following vice-presidents of the Sections for 1947: Mathematics (A), Robert Lee Moore, University of Texas; Physics (B), Merle A. Tuve, Carnegie Institution of Washington; Chemistry (C), Farrington Daniels, University of Wisconsin; Astronomy (D), Dean B. McLaughlin, University of Michigan; Geology and Geography (E), Marland P. Billings, Harvard University; Zoological Sciences (F), Franz Schrader, Columbia University; Botanical Sciences (G), W. F. Loehwing, University of Iowa; Anthropology (H), Wilson D. Wallis, Heathside Inn, Craftsbury Common, Vermont; Psychology (I), Edna Heidbreder, Wellesley College; Social and Economic Sciences (K), Frederick Stephan, Cornell University; History and Philosophy of Science (L), F. S. C. Northrop, Yale University; Engineering (M), Gordon M. Fair, Harvard University; Medical Sciences (N), E. V. Cowdry, Washington University Medical School; Agriculture (O), William H. Alderman, University of Minnesota; and Education (Q), W. A. Brownell, Duke University.

Two members of the Executive Committee, elected for terms of four years, were George A. Baitsell and Kirtley F. Mather, according to the announcement which pointed out that the new constitution does not provide for elected members of the Council, although under the old constitution eight members of the Council were elected from the fellows of the Association, two each year for terms of four years. On recommendation of the Executive Committee, the Council voted that the eight members of the Council elected under the old constitution be continued until expiration of their terms.

About People

Mark F. Boyd will retire from the staff of the International Health Division, Rockefeller Foundation, at the end of January after 25 years of service. In 1931 he became director of the Malaria Research Station, Tallahassee, Florida, where he worked with naturally induced malaria.

Howard Lawton Knight, editor in chief of the *Experiment Station Record* of the U. S. Department of Agriculture, retired December 31 after 42 years of continuous service in the Department. He first went with the *Experiment Station Record* in 1906 when he was made assistant editor. He took part in the 1934 revision of *Webster's New International Dictionary.*

Martha C. Gundlach, who has prepared more than 50 indexes for the *Experiment Station Record*, retired at the same time as Mr. Knight.

Aaron Edwin Margulis was recently promoted to professor of bacteriology in the New York Post-Graduate Medical School and Hospital. The appointment, which follows the death of Ward J. MacNeal, carries the titles of executive officer of the Department of Bacteriology and director of the Hospital and Dispensary Services of Bacteriology.

Kenneth A. Norton has been made chief of the recently established Frequency Utilization Research Section of the Central Radio Propagation Laboratory, National Bureau of Standards. Mr. Norton rejoined the Bureau from the War Department where he served during the war as a consultant in radio propagation to the Chief Signal Officer and assistant director of W. L. Everitt's Operational Research Group.

George Tunell, on leave from the Geophysical Laboratory, Carnegie Institution, of Washington, until June 30, 1947, is serving as acting associate professor of mineralogy and metalliferous geology at the California Institute of Technology. The position was formerly occupied by H. J. Fraser, who resigned to become general manager of the Falconbridge Nickel Company.

Cdr. Horace C. Dudley was appointed head of the Biochemical Section, Naval Medical Research Institute, Naval Medical Center, Bethesda, Maryland, on his return to civilian status. During the war Cdr. Dudley served as an ammunition and explosive specialist and, more recently, was officer-in-charge, Naval Explosives Unit, for Operation Crossroads. Before the war Cdr. Dudley was with the National Institute of Health.

Ralph W. Lewis, on sabbatical leave as associate professor of biology from Michigan State College, will be at the California Institute of Technology until July 1, conducting postdoctorate research under the direction of G. W. Beadle.

Albert Milzer, formerly research virologist, Samuel Deutsch Serum Center, has been appointed director of the Department of Bacteriology, Michael Reese Hospital, Chicago.

Gordon L. Walls was made an associate professor of physiological optics in the School of Optometry, University of California, Berkeley, effective January 1. Prior to this time, Dr. Walls was research associate with the Bausch & Lomb Optical Company.

I. Newton Kugelmass has been appointed consultant nutritionist to the Department of Health and the Department of Hospitals, New York City.

Courtland L. Butler, Jr., has been named chief of the Information Division, Technical Command, Edgewood Arsenal. Dr. Butler, previously with the Research and Development Division, Office, Chief Chemical Corps, Washington, has specialized in sugars and their derivatives and chemotherapy of pneumonia.

Robert Davis, Department of Psychiatry, University of Colorado School of Medicine, Denver, has been appointed associate professor of neuropsychiatry, University of Texas Medical Branch, Galveston, and assistant director of the Galveston State Psychopathic Hospital.

Charles S. Bridgman has been promoted from assistant professor to associate professor of physics and astronomy, at Ohio State University.

Thomas Sproston, Jr., formerly Massachusetts State College, has been appointed assistant professor of plant pathology, University of Vermont, and assistant plant pathologist, Vermont Agricultural Experiment Station.

B. E. Dahlgren, chief curator of the Botany Department, Chicago Natural History Museum, retired January 1. He will be succeeded by Theodor Just who joined the staff last August as associate curator. Mr. Dahlgren was a member of the Botany staff since 1909 and chief curator since 1924.

John N. Belkin has been appointed head of the Biology Department of Mohawk College, Utica, one of the Associated Colleges of Upper New York, opened this fall especially for veterans.

Dr. Belkin served 39 months in the U. S. Army, where he worked on malaria control in the Asiatic-Pacific theater, and also was Russian interpreter for Headquarters, Armed Forces Pacific Area Command.

Otto E. Guttentag, on temporary leave of absence from the University of California Medical School, has been appointed Consultant in Medical Education in Germany. His address for communications dealing with problems of medical education in Germany is: Otto E. Guttentag, Higher Education and Teacher Training Section, OMGUS, A.P.O. 742, c/o P.M., New York, New York.

H. Radclyffe Roberts, assistant curator of Insects, and member of the Scientific Council and Board of Trustees of the Academy of Natural Sciences, Philadelphia, has been appointed managing director, it has been announced by Charles M. B. Cadwalader, president. Dr. Roberts, with the Academy for about 20 years, served during the war in the Medical Department of the Army and with Edward S. Ross, California Academy of Sciences, produced the mosquito atlas used by the armed forces in combating malaria. He has collected and made field studies in Africa, New Guinea, the Philippines, Hawaii, Mexico, Trinidad, as well as the United States.

Joseph P. Weinmann, Loyola University School of Dentistry, has been appointed associate professor of histology, University of Illinois College of Dentistry.

Grants and Awards

Scientists of all countries have been invited to compete in the next four years for prizes totaling $40,000, a fund established by the Sugar Research Foundation and administered by the National Science Fund, National Academy of Sciences. Established to stimulate scientific studies of sugar as a food and industrial raw material, awards of $5,000 will be given in 1947, 1948, and 1949, with a grand prize of $25,000 in 1950 for the most significant discovery of the preceding five years, Harlow Shapley, chairman of the National Science Fund announced. Winners of the preliminary awards are also eligible for the grand prize.

In discussing rules governing the award, Dr. Shapley remarked that 44 projects dealing with physiological, chemical, and industrial aspects of sugar and its derivatives are being sponsored at universities under the direction of Robert C. Hockett, scientific director, Sugar Research Foundation, through grants-in-aid of more than $500,000. The Foundation, supported by sugar producers and processors of the United States, Cuba, Canada, Puerto Rico, and the Dominican Republic, has been engaged since its formation in 1943 in collating and publishing existing information about sugar.

Entries for the 1947 prize must be in the hands of the Executive Secretary of the National Science Fund, National Academy of Sciences, Washington 25, D. C., no later than February 1.

Members of the Advisory Committee in charge of recommendations for the award include: A. Baird Hastings, Harvard University; Charles F.Kettering, General Motors Corp.; Carl S. Marvel, University of Illinois; Edmund W. Sinnott, Yale University; William C. Stadie, University of Pennsylvania; and Vincent du Vigneaud, Cornell University Medical College. The 1946 prize was awarded recently to W. Z. Hassid, H. A. Barker, and M. Doudoroff, University of California, for the enzymatic synthesis of crystalline sucrose.

The Committee on Scientific Research of the American Medical Association has made the following grants for 1947:

Wesley Spink, University of Minnesota, brucellosis; Catharine Macfarlane, Women's Medical College of Pennsylvania, value of periodic pelvic and breast examinations for cancer; L. R. Cerecedo, Fordham University, vitamin B deficiencies in rats and mice; Reuben Mokotoff, Montefiore Hospital, New York, relation to edema of renal clearance in congestive heart failure; James H. Leathem, Rutgers University, antihormones; George Sayers, University of Utah, pituitary adrenocorticotropic activity; Paul F. Hahn, Vanderbilt University, radioactive manganese in Hodgkin's disease, Leukemia, lymphoma; Bernard N. E. Cohn, National Jewish Hospital, Denver, experimental bone tuberculosis; Harold J. Harris, New York, diagnosis and treatment of brucellosis; Rollin A. Daniel, Jr., and F. T. Billings, Vanderbilt University, atabrine in the treatment of tuberculosis; Hans Popper, Cook County Hospital, Chicago, morphology of the liver in relation to function; Frederick H. Howard, Lincoln Hospital, New York, vectocardiographic research; Archie R. Tunturi, University of Oregon, acoustic system of the dog; Hovey Jordan, University of Vermont, project method in the teaching of histology; Rachmiel Levine, Michael Reese Hospital, Chicago, secretion and metabolism of progesterone in threatened abortion; A. M. Lassek, Medical College of South Carolina, degenerative phenomena in the pyramidal tract.

Colleges & Universities

Zoologisches Institut, Universität, Vienna I, Austria, was three-fourths destroyed, but the collection and library are almost completely preserved, according to a letter from Felix Mainx, formerly assistant professor of plant physiology and genetics at the German University of Prague, and now at the Institut. Technical equipment and genetic material were lost, and current literature is lacking. Reprints on genetics and plant physiology sent to the above address would be appreciated, the letter indicates.

B. F. Skinner, professor of psychology, University of Indiana, will be William James Lecturer in Psychology at Harvard University during the fall term of 1947. Prof. Skinner, fifth psychologist to hold the appointment, will discuss the psychological analysis of verbal behavior in a series of 10 weekly lectures. During the period he will also offer a graduate seminar on the principles of behavior.

Previous William James Lecturers in Psychology have been John Dewey, Wolfgang Köhler, Kurt Goldstein, and E. L. Thorndike.

The new Research Division, Department of Student Life, College of the City of New York, is engaged in an intensive study of the effectiveness of entrance examinations, the results of which will be published by Frank K. Shuttleworth, director of the Division.

The University of Minnesota has accepted a gift of $15,000 to establish the Conway MacMillan Memorial Research Fellowship in Botany and has chosen as first recipient of the $1,200 annual award A. Stanley Holt, graduate student at the University of Minnesota working on the evolution of oxygen by chloroplasts in the presence of oxidizing agents. The gift was presented by Charles J. Brand, former student of Prof. MacMillan and for many years active in the U. S. Department of Agriculture and the trade association field. The donor provides that the principal sum and the interest be spent in 5 years.

Prof. MacMillan was for almost 40 years head of the Department of Botany, University of Minnesota, beginning

1887, and an active teacher, writer, and researcher in his field. In 1899, according to the donor, he originated the idea of popping other grains as popcorn is popped, a process later patented by a colleague, who continued the experimentation.

The research fellowship is available annually to doctoral students in botany who have their Master's degrees from the University of Minnesota or institutions of similar standing. In the terms of the gift, special mention is accorded those from the University of Chile and the Catholic University of Chile.

Instituto de Pesca del Pacífico has been founded at Guaymas, Sonora, Mexico (Apartado Postal No. 34), according to René Núñez, who has begun research there on the biology and fisheries of the Mexican west coast. Señor Núñez studied at Stanford University under a Fish and Wildlife Service fellowship.

Meetings

The American Academy of Oral Pathology will hold its first annual meeting at the Stevens Hotel, Chicago, February 9. The Academy, organized to promote interchange of ideas in oral pathology, advance sound scientific procedures in clinical dentistry, and stimulate research and teaching, was organized by the Registry of Dental and Oral Pathology of the American Dental Association at the Army Institute of Pathology. Applications for membership may be made through the secretary, Lt. Col. Joseph L. Bernier, Army Institute of Pathology, Washington 25, D. C.

More than 40,000 metal scientists, engineers, and executives are expected to attend the fifth Western Metal Congress and Exposition to be held in the two Oakland, California, Civic Auditoriums in the San Francisco-Oakland area for six days beginning March 22.

Sixteen western divisions of the following technical societies are actively cooperating in the activities of the Congress: American Society for Metals, sponsors of the event; American Chemical Society; American Foundrymen's Association; American Industrial Radium and X-Ray Society; American Institute of Mining and Metallurgical Engineers; American Institute of Electrical Engineers; American Society for Testing Materials; American Society of Tool Engineers, Inc.; American Welding Society; Mining Association of California; Northwest Electric Light and Power Association; Pacific Coast Electric Association; Purchasing Agents Association of California, Inc.; Society of Automotive Engineers; Western Oil and Gas Association; and the American Petroleum Institute.

Further information may be obtained from W. H. Eisenman, managing director, W.M.C.E., Hotel Leamington, Oakland, California.

Alpha Epsilon Delta, national honorary premedical fraternity, in cooperation with the University of Louisville will bring together faculty members from more than 100 colleges and universities at a conference on premedical education in Louisville February 21–22. The program, for institutions in Indiana, Illinois, Kentucky, Michigan, and Ohio, will include one session on the basic sciences and another on social sciences and humanities in relation to medical education. Inquiries may be addressed to Dr. Hugh E. Setterfield, School of Medicine, Ohio State University, Columbus 10, Ohio.

The Natural Resources Council of America was organized at Mammoth Cave, Kentucky, October 25–26, "to advance attainment of sound natural resource management in the public interest," according to Howard Zahniser, representing the Wilderness Society. The functions of the Council as set forth in a program adopted unanimously at the October meeting "shall be to effect closer cooperation and coordination of member organizations . . . make available to member organizations scientific data and other information to aid them in intelligent determination of conservation problems."

Organizations represented at the meeting were National Audubon Society, Friends of the Land, Wildlife Management Institute and American Wildlife Foundation, American Nature Association, Ecological Society of America and Limnological Society of America, Izaak Walton League of America, National Wildlife Federation, National Parks Association, and the Wilderness Society.

Elections

The Emory Chapter of Sigma Xi, Emory University, Georgia, has elected the following officers for 1947: Howard M. Phillips, president; James L. Morrison, vice-president; Charles T. Lester, treasurer; A. C. Munyan, custodian; and Robert Lagemann, secretary.

The American Mathematical Society at its annual meeting in Swarthmore, Pennsylvania, December 28, elected Einar Hille, Yale University, president; P. A. Smith, Columbia University, vice-president; J. R. Kline, University of Pennsylvania, secretary; T. R. Hollcraft, Wells College, associate secretary; and B. P. Gill, College of the City of New York, treasurer.

The Genetics Society of America has elected the following officers for 1947: H. J. Muller, president; L. H. Snyder, vice-president; and M. R. Irwin, secretary-treasurer.

Shell Development Research Club, affiliated with Sigma Xi, elected for 1947, Fred H. Stross, chairman; Harold T. Byck, past chairman; Robert G. Larsen, chairman-elect; Bradford P. Geyer, secretary; and T. Kirk Miles, treasurer.

The Botanical Society of Washington, D. C., has elected the following officers for 1947: Harry R. Fulton, president; Eugene A. Hollowell, vice-president; Elmer C. Stevenson, recording secretary; Anna E. Jenkins, corresponding secretary; Wilbur D. McClellan, treasurer; Lee M. Hutchins and Ronald Bamford, counsellors; John A. Stevenson, archivist; and L. Edwin Yocum, representative to the Washington Academy of Sciences.

The U. S. Department of Agriculture announced on November 25 the successful commercial application of its development for making bristles from casein. Louis B. Howard, chief of the Bureau of Agricultural and Industrial Chemistry, stated that research on the new product was initiated four years ago at its Eastern Regional Research Laboratory, Philadelphia, to find a suitable substitute for imported natural bristle. The artificial fiber, developed by Thomas L. McMeekin and associates, attracted the interest of numerous companies, and one of these, The Rubberset Company of Newark, is opening a new factory at Salisbury, Maryland, for the manufacture of casein bristle and brushes, using the process developed by the Department scientists. The artificial bristle is made by

extrusion of a mixture of casein and water through a suitable die, after which it is subjected to finishing operations. The final product is round in cross-section and has a black color comparable to that of horsehair or pig bristle. Like other artificial fibers, it can be produced in any length desired and in a range of diameters. Of many possible uses, the bristle is particularly adapted to the construction of paint brushes, since it is resistant to oils and organic solvents.

The National Registry of Rare Chemicals, Armour Research Foundation, 35 West 33rd Street, Chicago 16, Illinois, indicates that the following chemicals are needed: 4-bromomethylazobenzene; 2-hydroxyhexyl aldehyde; 2-hexen-1-ol; pulegone; thujone; tetrabromo-xylene; 1,3-pentanediol; cyclobutadiene; 3-amino-2,4-dimethylbenzoic acid; aluminum borotartrate; indican; stearolic acid; behenolic acid; d-camphor; l-menthol; carbonyl cyanide; di-o-tolyl zinc; 2,2′,2″-tripyridyl; 1,1,1,2,3-pentachloroisobutane; 1,1,2,3-tetrachloroisobutane. Communications regarding these should be directed to the Registry at the address given above.

Chronica Botanica has recently issued its first monthly newsletter supplement, *Biologia*, designed to report quickly on biological developments of professional and international interest. The format of *Biologia* is based on a copy of the Massachusetts Centinel of 1786. The newsletter, which will carry short items rather than discussions or articles, will be sent to subscribers of *Chronica Botanica* free and is available to others at the rate of $4.00 for two years.

The U. S. Civil Service Examiners, Philadelphia Quartermaster Depot, have announced examination for the position of chemist, salary range $4,902 to $7,102, for duty at the Philadelphia Quartermaster Depot and other agencies in the Third Civil Service Region. Duties of the positions involve chemical research and development. Applicants, who will be rated on the basis of their experience and training, must submit applications to the Executive Secretary, Board of U. S. Civil Service Examiners, 2800 S. 20th Street, Philadelphia 45, Pennsylvania, not later than February 6.

The Chicago Natural History Museum is currently showing "The Incas," an exhibit of 32 large photographs by Frank Scherschel, photographer for *Life*, who spent many weeks in Peru exploring and photographing traces of the Inca civilization. The exhibit, recently displayed at the New York American Museum of Natural History and the Metropolitan Museum of Art, will continue in Chicago through January 19.

The photographs were taken for the most part in the Urubamba Valley and include the ruins of Fort Sacsahuaman, the hillside village of Winay Wayna, explored in 1941, Ollantaytambo, and Machu Picchu. Thirteen of the panels are devoted to Machu Picchu, one of the best preserved of the Inca cities.

Mendel's manuscript, "Versuche über Pflanzen Hybriden," it is reported, was removed from the Natural History Society, Brno, Czechoslovakia, by a German professor at the time of the Russian occupation. The report comes from Herbert C. Hanson, chief, Agricultural Division, UNRRA Mission to Czechoslovakia, who, in communication with Dr. Jaroslav Kříženecký, Zootechnical Research Institute and College of Agriculture, Brno, learned that Otto Richter, German professor who took over the chair of plant physiology in the Masaryk University and assumed charge of the quarters of the Natural History Society, carried Mendel's manuscript about with him in his briefcase. When the Germans evacuated, Richter disappeared and, it is thought, took the manuscript with him to Germany or Vienna. To date, though search has been made, it has not been found.

The manuscript had been at the Natural History Society in Brno since 1910, when it was found by Prof. Hugo Iltis in a wastepaper basket in the library of the Society.

Recent Deaths

Edgar Lee Hewett, 81, archaeologist, died December 31 at Albuquerque, New Mexico, where he was director of the Museum of New Mexico at the time of his death. Since 1906 Dr. Hewitt had been director of American research for the Archaeological Institute of America; since 1907, director of the American School of Archaeology, now the School of American Research, and president of its Executive Board since 1930. Between 1923 and 1930 he took part in expeditions in Palestine, Syria, Arabia, Mesopotamia, Morocco, Algeria, Tunisia, and the Sahara. He also directed excavations in Guatemala and the southwestern United States.

Eugene Charles Rowe, 76, formerly head of the Department of Psychology and Education, Central State Teachers College, Mt. Pleasant, Michigan, died at St. Petersburg, Florida, December 31.

Johann Georg Koenigsberger, 71, professor emeritus, University of Berlin, died December 3 in Freiburg, Breisgau.

Princeton Bicentennial

A conference on the "Problems of Mathematics," one of a series in celebration of the bicentennial of the founding of Princeton University, was held at Princeton December 17–19. There were, in addition to local mathematicians, 76 other participants, 12 of whom came from outside the United States.

The conference was organized in the form of nine round tables on various subjects, with the discussion oriented as far as possible toward formulation of problems for future work. The sessions were as follows: Algebra—chairman, E. Artin; reporter, G. P. Hochschild; discussion leaders, G. Birkhoff, R. Brauer, N. Jacobson; Algebraic Geometry—chairman, S. Lefschetz; reporter, I. S. Cohen; discussion leaders, W. V. D. Hodge, O. Zariski; Differential Geometry—chairman, O. Veblen; reporter, C. B. Allendoerfer; discussion leaders, V. Hlavatý, T. Y. Thomas; Mathematical Logic—chairman, A. Church; reporter, J. C. C. McKinsey; discussion leader, A. Tarski; Topology—chairman, A. W. Tucker; reporter, S. Eilenberg; discussion leaders, H. Hopf, D. Montgomery, N. E. Steenrod, J. H. C. Whitehead; New Fields—chairman, J. von Neumann; reporter, V. Bargmann; discussion leaders, G. C. Evans, F. D. Murnaghan, J. L. Synge, N. Wiener; Mathematical Probability—chairman, S. S. Wilks; reporter, J. W. Tukey; discussion leaders, H. Cramér, J. L. Doob, W. Feller; Analysis—chairman, S. Bochner; reporter, R. P. Boas; discussion leaders, L. V. Ahlfors, E. Hille, M. Riesz, A. Zygmund; Analysis in the Large—chairman, M. Morse; reporter, M. Shiffman; discussion leaders, R. Courant, H. Hopf. It is planned to issue shortly a descriptive pamphlet, and later a more complete monograph, covering the work of the conference. The monograph will contain an extensive list of the problems proposed.

TECHNICAL PAPERS

The Polished Rocks of Cornudas Mountain, New Mexico

WALTER B. LANG

U. S. Geological Survey, Washington, D. C.

In 1941 (*1*) I presented my recollections and inferences concerning certain polished surfaces I had noticed on the porphyritic rocks of the Hueco and Cornudas Mountains in Texas and New Mexico. Lately I had opportunity to give more than casual attention to the appearance and relation of the polished surfaces to the rocks on which they are found about Cornudas Mountain.

Both Cornudas Mountain and the Hueco Tanks, which lie along the western Texas and New Mexico boundary and are about 35 miles apart, are plugs or laccolithic intrusions injected into Permian strata from the same igneous magma. The rock is a porphyritic syenite composed of potash feldspar with a small amount of plagioclase, and hornblende, amphibole, biotite, and magnetite. Fresh specimens of the rock range in color from a faint pink to a pale gray, depending on the inherent color of the feldspar. Weathering of the rock frees iron from the ferromagnesian minerals, and a coating of hydrous iron is formed over the weathered surface of the rock which imparts to it a dark reddish-brown color and causes the mountain to glisten in the sun like copper-bronze.

The natural rupture of the rock, either by fracture or spalling, produces a roughened, hackly surface. The fracture tends to pass around rather than through the phenocrysts of feldspar. Thus, the feldspars commonly stand out as much as an eighth of an inch or more above the general level of the rock surface. Spotted over this natural roughened surface of the rock are occasionally to be found highly polished areas. These polished surfaces were seen only on the southeast side of Cornudas Mountain and only within a relatively narrow zone where the coarse rock talus at the base of the cliffs meets the detrital apron. Some enormous blocks of rock have fallen from the cliffs and tumbled out to isolated positions on this surrounding and flat-lying detrital apron. Most of these boulders show some evidence of polish.

Often within the center of a polished area covering 5 to 25 square feet of rock there are no irregularities—only a smooth, glassy surface. This highly polished surface grades outward into a normal rough rock surface through a marginal zone wherein the phenocrysts stand out like rounded and polished cameo buttons in a rough, granular, intaglio background. Thus, a gradation in the state of perfection of the polish is displayed. In the marginal zone the projections of the phenocrysts are progressively less rounded off outward, and the depressions have received no polish where the higher protrusions are not well worn down. It is evident that the polish is due to lapping by a flexible medium which was capable of following to some degree the irregularities of the original surface and thus extending the buffing process somewhat into the recessed parts of the surface. Only one agency is likely to have produced such an effect upon these rocks: It is a common habit for grazing animals to choose certain places to scratch their hides. The hides of animals contain oily matter, and this, when combined with the fine dust which animals habitually toss upon themselves, forms an effective abrasive capable of wearing away rock and producing a high polish.

An examination in section of the polished surface shows a thin discoloration band, extending an average of $\frac{1}{50}$ inch in depth, which is apparently due to absorption of animal fat. It is different in appearance from that due to the staining by hydrates of iron. To determine the presence of oil or fat, a piece of the rock having 4 square inches of polished surface was submitted to W. W. Brannock, of the Chemical Laboratory, Geological Survey, for test. The material was treated with carbon bisulfide after being broken into coarse fragments, and the solvent was evaporated in a porcelain dish. For even so small an area of polished surface as that borne by this piece of rock a very sizable spot of honey-yellow oily matter remained on the porcelain dish. A blank test of the carbon bisulfide proved that oily matter had been extracted from the rock. The associated brown stain was also chemically proved to be an iron compound.

Under low-power magnification a shriveled coating of an amber-colored substance was repeatedly observed on the surface of the highly polished feldspar phenocrysts. This material had the appearance of a dried-out oil film, but both flame and heat tests failed to show any expected results. The material proved refractory. Microscopic examination disclosed that it is isotropic and is silica in the form of opal. From these facts it is deduced that the fine silica dust mixed with oily fats was rubbed on the surface of the rocks by animals, and that in the decades, if not centuries, of exposure to the elements since the last animal used the rock for a rubbing post, the silica weathered to opal, and the oil gradually vanished from the surface film. As the oil distilled away in the heat of the sun, the film shrank, and the residuum of opal formed a shriveled and mummified skin on the face of the feldspar phenocrysts.

These few facts seem convincing evidence that the polished surfaces of rock about Cornudas Mountain are of animal origin.

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Vitamin C Content of Mexican Ornamental Plants

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It is known that the leaves or flowers of certain inedible ornamental plants are very rich in vitamin C: 600 mg./100

grams fresh substance in the lily (*1*); more than 10,000 mg./100 grams dry substance in gladioli (*7*); 900 mg./100 grams fresh substance (*5*) or 6,000 mg./100 grams dry substance (*2*) values found in each case to the dry basis.

All the plants selected are ornamental flowers common in Mexico, D. F., and were analyzed the same day they were

TABLE 1

Botanical name	English name	Part of plant	Month gathered	Fresh substance		Total solids (%)	Dry substance	
				Ascorbic acid (mg./100 grams)	Ascorbic acid + dehydro-ascorbic acid (mg./100 grams)		Ascorbic acid (mg./100 grams)	Ascorbic acid + dehydro-ascorbic acid (mg./100 grams)
Althaearosea	Hollyhock	Petals	June	64.6	73.3	18.7	344.3	391.9
Bellis perennis	True or English daisy	"	May	37.4	40.4	14.9	251.0	271.1
Bouvardia longiflora		"	June	90.3	91.7	11.5	785.2	797.3
Centaurea Cyanus	Cornflower or bachelor's-button	"	May	79.5	81.2	16.7	476.0	486.2
Dianthus Caryophyllus	White carnation or clove pink	"	April	126.4	131.5	16.0	790.0	821.8
	Red carnation or clove pink	"	"		136.2	15.6		873.0
Gardenia augusta	Gardenia	"	June	49.0	59.4	17.0	288.2	349.4
		Leaves	"	135.5	143.0	34.8	389.3	410.9
Gladiolus byzantinus	Gladiolus, white	Petals	"	118.3	122.0	6.3	1,877.7	1,936.5
		Leaves	"	52.8	55.8	27.9	189.2	200.0
		Stalks	"	134.0	135.2	14.7	911.5	919.7
Hydrangea Hortensia	Hydrangea	Petals	"	36.4	44.2	23.9	152.3	184.9
		Leaves	"	27.3	34.3	13.9	196.4	246.7
Lathyrus odoratus	Sweet pea, white	Petals	May	72.9	74.4	13.6	536.0	547.0
Lilium candidum	Madonna lily	"	"	45.6	50.5	8.4	542.8	601.2
		Leaves	"	53.4	55.3	13.2	404.5	418.9
		Stalks	"	29.7	34.1	15.4	192.8	221.4
Philadelphus mexicanus	Mock-orange	Petals	"	35.7	37.1	12.9	276.7	287.6
Rosa centifolia	Cabbage rose, white	"	"	64.9	75.4	17.4	372.9	433.3
		Leaves	"	11.4	17.1	32.0	35.6	53.4
Rosa fragans	Tea rose	Petals	June	91.2	106.6	17.2	530.2	619.8
Zantedeschia aethiopica	Calla lily	"	April	90.8	97.6	13.4	677.6	728.3
		Leaves	"	109.4	113.0	20.2	541.5	559.4
		Stalks	"	11.1	15.6	6.3	176.2	247.6

in *Primula officinalis;* and lesser quantities in other flowers (*4*, *6*).

The extraction of vitamin C from gladioli has been included in the subject matter of industrial patents (*8*).

As a contribution to the knowledge of the distribution of vitamin C in inedible plants, we have determined its content in ornamental Mexican plants, by the colorimetric method, using 2,6-dichlorophenol indophenol, determining in each case ascorbic acid alone and the total ascorbic acid plus dehydroascorbic acid by the usual method of reduction with H_2S after precipitating with mercuric acetate (*3*).

In each case we have indicated the part of the plant analyzed and the month in which it was collected. We have determined also the per cent of total solids and have recalculated the two gathered. The results obtained are reported in Table 1.

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Experimental Argyrosis: II. Treatment of Rats Receiving Silver With 2,3-Dimercaptopropanol (BAL)

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In a previous communication (*3*) it has been reported that silver pigment is deposited in the experimental rat in a way essentially similar to that in which it is deposited in man. In view of the efficacy of 2,3-dimercaptopropanol (BAL) in the treatment of poisoning with arsenic (*1, 4*) and mercury (*2*), it appeared desirable to study the effect of this agent on the experimental argyrosis of the rat.

The experiment was carried out on four rats, grouped in pairs and placed on a diet of dog pellets. The first pair received a solution of 1:1,000 silver nitrate in place of drinking water for a period of 456 days. During this time a total amount of 23.2 grams of silver nitrate was consumed by the two animals, or an average of 11.6 grams each. On the 457th day the silver nitrate solution was discontinued and replaced by water. At this time the eyes of both rats were distinctly pigmented, one slightly more so than the other. Eighteen days later the more deeply stained rat was started on treatment with intramuscular BAL. The BAL was given in a 1:50 dilution in cottonseed oil. A total of nine injections was given on alternate days, covering a period of 18 days. Each single dose was 0.2 mM/kg. (10 times the minimal effective dose for the treatment of acute arsenic poisoning in the cat). The other rat was maintained as a control. The treated animal showed a weight loss of 30 grams over the period of therapy, but otherwise appeared healthy. The control animal lost 6 grams. Both animals were sacrificed on the 21st day, at which time the eyes of the treated rat were still darker than those of the control.

On histological examination, the eyes, thyroid, liver, pancreas, spleen, and kidneys contained an apparently identical amount of silver deposit. No lesions were found in either rat.

The second pair of rats received for a period of 514 days a 1:1,000 solution of silver chloride with added sodium thiosulfate (approximately 1:300) in place of drinking water. The total average silver chloride intake for each of the two animals was 12.9 grams. On the 515th day the silver chloride solution was replaced by drinking water. The eyes of the pair were also distinctly pigmented. Eighteen days later the more deeply stained rat was started on BAL therapy. The dose and manner of administration was as described above, with the exception that a total of 18 injections of BAL was given, covering a period of 38 days. The cage mate was kept as a control. During the period of treatment the treated animal lost 25 grams in weight, but otherwise appeared healthy; the control showed a 3-gram gain. On the 42nd day both were sacrificed, at which time the eyes of the treated rat still appeared darker than those of the control.

On histological examination, there were apparently identical amounts of silver deposits in the thyroid, kidneys, eyes, and choroid plexus of each rat. There were no lesions indicating any toxic effect in either rat.

It appears from these observations on a limited number of animals that BAL is incapable of mobilizing silver, which is deposited in the tissues as metallic silver or silver oxide. It seems likely, therefore, that BAL should prove of little or no value in the treatment of argyria in man. It is interesting to note the marked resistance of the rat to poisoning by BAL. No acute symptoms resulted from the injection of 0.2 mM/kg., and there were no chronic effects from the repeated administration of this quantity of BAL.

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The Movement of Substances Through a Two-phased Solution System[1]

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A thermodynamically sound treatment is essential to an understanding of the movement of substances through solutions. Manifestations of flux are common in aqueous biological systems. These phenomena are logically expressed on the basis of the concept of escaping tendency or free energy of a constituent component. Certain fundamentals of the process are presented in the hope that the free-energy concept, as it applies to this movement, will be adopted generally by biologists. The tendencies for movement of water will be discussed first, followed by that of a solute in an aqueous solution system.

WATER MOVEMENT

Pure water possesses an internal energy representing the sum of its internal kinetic and potential energies. At thermodynamic equilibrium, a steady state, the free energy of the water is equal throughout the phase. The free energy or escaping tendency of the water molecules may be modified by the application of certain chemical or physical influences. The addition of a solute to water lowers the free energy of the solvent in the resultant solution. The application of a pressure to water increases its free energy. At thermodynamic equilibrium within a solution consisting of two components,

[1] Detailed treatises will be printed in *Botanical Review* (1947), comprehending the movement of water and of a solute. In these, references are made to earlier publications pertinent to the subject.

Symbols used are defined as follows: p is an applied pressure, in a given state of the system, necessary to make $\bar{f}$ equal to $\bar{f}^o$; p^o is an applied pressure, in a reference or standard state of the system; $\bar{f}$ is the partial molal free energy of a constituent component of a solution in a given state; $\bar{f}^o$ is the partial molal free energy of a constituent component of a solution in a reference or standard state—here, at infinite dilution; $\bar{v}^o$ is the partial molal volume of a constituent component of a solution in a reference or standard state—here, at infinite dilution; F is a specific (volumed) free energy of a constituent component of a solution in a given state; subscripts i and e refer to the separate phases of a two-phased solution system—here, internal and external, respectively; and subscripts (Δf) or ($-\Delta f$) refer to influences in or on a system, which increase or decrease, respectively, the free energy of a constituent component of a solution from that in a reference or standard state to that in a given state.

solvent water and a single solute, the free energy of each component is equal throughout the phase. If each component, the water or the constituent solute, is not at thermodynamic equilibrium throughout the phase, it will work itself through the solution toward equality of escaping tendency, in accordance with the difference in free energy. Here, this process is called a flux, the term diffusion being employed where migration is restricted to a response to a difference of concentration or activity of a constituent component in solution within a system.

In practice, the free energies themselves are not measured, but the *difference* in free energy of the component between that in the given state and that in a reference or standard state is determined. Gauging the pressure difference which would be necessary to adjust the free energy of the water from that in the given state to that in a reference state serves as a measure of the free-energy difference under the two conditions. In dilute solutions, where the free-energy difference of the water is due only to the presence of solute in the solution, these pressures and free energies are equated approximately through the relation,

$$p - p^0 = \frac{-(\bar{f} - \bar{f}^0)}{v^0} = F. \qquad (1)$$

Where pressure is imposed on the medium, as a single factor contributing to the free-energy difference of the water, the equation takes the form,

$$-(p - p^0) = \frac{(\bar{f} - \bar{f}^0)}{v^0} = F. \qquad (2)$$

The only difference between Equations 1 and 2 is that of algebraic sign. The net effect of those influences which decrease the free energy of water and those which increase the free energy in a single phase may be expressed by the equation,

$$\Sigma F_{(-\Delta f)} - \Sigma F_{(\Delta f)} = \frac{-(\bar{f} - \bar{f}^0)}{\bar{v}^0}. \qquad (3)$$

The pressure which must be applied to make the free energy of water in a given state equal to that in a reference state may be conveniently observed by a two-phased system in which a semipermeable membrane, permeable to the water, is interposed. The difference in pressure which must be applied to the two phases to bring about thermodynamic equilibrium for water across the interposed membrane is a measure of the free-energy difference of the water between the two phases. The specific (volumed) free energy (F), numerically equal to the partial molal free-energy difference divided by the partial molal volume of the water, is likewise a measure of the free-energy difference. Moreover, it expresses the thermodynamic viewpoint of the escaping tendency of the water from one phase to the other in physically measurable dimensions, namely, pressures. These may be converted to dimensions of energy by means of a coefficient, namely, the partial molal volume of the constituent component at infinite dilution of the solution.

It is of interest to know whether water will tend to migrate from one phase (external) to the other (internal) due to a possible difference in free energy of the water, schematically represented by the formula,

$$H_2O \text{ (external)} \xrightarrow{\text{influx}} H_2O \text{ (internal)}. \qquad (4)$$

The measure of the tendency for water to move is given by the difference between the free energy of the water in the internal phase and that in the external phase of the osmoscope, namely, $(\bar{f}_i - \bar{f}_e)$. If this difference is negative in sign, water will tend to migrate inward, as written in the previously cited formula (4). If the quantities $(\bar{f}_i - \bar{f}^0)$ and $(\bar{f}_e - \bar{f}^0)$ are determined, then the difference between these values is $(\bar{f}_i - \bar{f}_e)$.

For a single phase, the net effect of those influences which decrease the free energy of water and those which increase the free energy was given by the relation,

$$\Sigma F_{(-\Delta f)} - \Sigma F_{(\Delta f)} = \frac{-(\bar{f} - \bar{f}^0)}{\bar{v}^0}. \qquad (3)$$

Then, for the two phases, the net influx specific free energy (NIF) is expressed by the equation,

$$(\Sigma F_{(-\Delta f)} - \Sigma F_{(\Delta f)})_i - (\Sigma F_{(-\Delta f)} - \Sigma F_{(\Delta f)})_e = \frac{-(\bar{f}_i - \bar{f}_e)}{\bar{v}^0} = \text{NIF}. \qquad (5)$$

Instead of expressing the specific free energies in groups relating to the two phases, i and e, respectively, they may be rearranged into categories representing the sums of the specific free energies tending to cause the water to move inward (influx, IF) and outward (efflux, EF) across the membrane. The net influx specific free-energy equation for water then becomes

$$\text{NIF} = \Sigma\text{IF} - \Sigma\text{EF} \qquad (6)$$

or, in more detailed form,

$$\text{NIF} = (\Sigma F_{(-\Delta f)i} + \Sigma F_{(\Delta f)e}) - (\Sigma F_{(-\Delta f)e} + \Sigma F_{(\Delta f)i}). \qquad (7)$$

The latter mode of expression has certain advantages when used in connection with graphic presentations of the specific free-energy and volume relations of an osmometer.

Solute Movement

By similar reasoning it may be shown that the fundamental principles of the tendencies for movement of solute are analogous to those discussed for water. The only differences in application of the general formulas relate specifically to the influence of the solute concentration of a solution on the specific free energy of a component. In the discussion of water movement the specific free energies referred to the solvent component. There, an *increase* in concentration of solute in a solution is accompanied by a corresponding *decrease* of the partial molal free energy of the water within the phase. For solute migration, the specific free energies refer to a constituent solute species in solution. In contrast, therefore, an *increase* in concentration of solute in a solution is accompanied by a corresponding *increase* of the partial molal free energy of the solute within the phase. In other words, the effect of a solute in solution is included here, in $F_{(\Delta f)}$ rather than in

$F_{(-\Delta f)}$ of Equations 3, 5, and 7. In this case, the symbol $\bar{v}^o$ refers to the partial molal volume of a constituent solute in solution.

Summary

The tendencies for movement of either solvent or solute in solution through a two-phased system are expressed in terms of specific (volumed) free energies. These are based on the concept of escaping tendency or free energy of a constituent component of a solution. This scheme is particularly useful to the biologist for evaluating the movement of water and solutes into cells or organs.

The Effect of Streptomycin on the Oxygen Uptake of *Eberthella typhosa*[1,2]

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During the course of investigations into the mode of action of streptomycin, it was found that the oxygen uptake of suspensions of washed cells of *Eberthella typhosa* was increased in the presence of streptomycin.

In 1934, Clowes and Krall (*2*) noted that dinitro compounds increased the oxygen uptake of sea urchin eggs, while apparently inhibiting cell division. In 1937, Clifton (*1*) found other substances which appeared to produce similar results in suspensions of bacteria and yeasts. Clifton took the view that such substances, which increased oxygen uptake and also interfered with certain cell functions, exerted their effects by inhibiting normal synthesis of cell components from the available substrate. In addition, he suggested that these substances might also favor oxidation of materials which had already been stored by the cell.

In this investigation oxygen uptake and respiratory quotients were measured in the Barcroft-Warburg apparatus. The phenomena which were observed resembled, at least superficially, those noted by Clowes and Krall and by Clifton. While the Hopkins strain of *E. typhosa* was used throughout most of this work, preliminary studies indicate that the results apply in general to other strains of *E. typhosa*, as well as to some other species of bacteria. With suspensions of the density used in this work it was found that streptomycin in a concentration greater than 500 units/ml. produced a change in oxygen uptake which was readily measurable and reproducible. Since the dry weight of bacteria per milliliter of suspension was approximately 3 mg., such a concentration of streptomycin is not unduly high.

Streptomycin, sufficient to make a final concentration of 1,000 units/ml., was added to a system in which endogenous respiration was proceeding at 37°C. in a phosphate buffer of pH 7.40. The result was an immediate and rather marked increase in the rate of oxygen uptake. After two hours had passed, the rate of uptake decreased until at six hours it was less than that of the controls, in which the rate of uptake remained constant for many hours.

The addition of glucose in a concentration of 0.01 per cent to a similar system also produced, of course, an increased rate of oxygen uptake. By the time that sufficient oxygen had been taken up to account for oxidation of about 65 per cent of the glucose as well as for endogenous oxidation, the rate of uptake had dropped to that of the controls. Further oxygen uptake occurred at this rate for many hours.

During the same time, when streptomycin in a concentration of 1,000 units/ml. was present as well as the glucose, sufficient oxygen was taken up to account for complete substrate oxidation as well as for oxidation due to the presence of a similar concentration of streptomycin in the system, which contained no available substrate. After this had occurred, oxygen uptake continued at a decreasing rate. When six hours had passed, the rate of uptake was less than that of the controls.

The evidence so far obtained indicates that the increase in oxygen uptake in the presence of streptomycin is not explainable on the grounds that the bacteria are bringing about the oxidation of the streptomycin or of impurities in it. Respiratory quotients are apparently increased 25 per cent by the addition of streptomycin to the previously described system, in which glucose is undergoing oxidation. In general, similar effects occur where other simple substrates are oxidized in the presence of streptomycin by the Hopkins strain of *E. typhosa*.

The effect of streptomycin on the oxygen uptake of a streptomycin-resistant variant of the Hopkins strain is of particular interest. This variant was produced by passing a subculture of the Hopkins strain through peptone water and increasing concentrations of streptomycin until it grew well in the presence of 1,100 units of streptomycin/ml. of peptone water. When glucose and streptomycin, the latter in a concentration of 500 units/ml., were both added to a suspension of the variant, the oxygen uptake was actually less than when glucose alone was added. When the streptomycin concentration was increased to 2,000 units/ml. under similar conditions, the oxygen uptake considerably exceeded the uptake which occurred when glucose alone was added.

When 500 units of streptomycin/ml. were added to suspensions of the variant in the absence of available substrate, no significant change in oxygen uptake occurred, but when the streptomycin concentration was increased to 2,000 units/ml., there was a considerable increase in oxygen uptake.

Preliminary studies of the biochemical changes produced in simple substrates by *E. typhosa* in the presence of streptomycin indicate that the presence of the antibiotic stimulates the production of changes which are compatible with the results observed in oxygen uptake studies. The utilization of carbohydrate substrate appears to be more complete and more rapid when streptomycin is present than when it is absent. It was found that streptomycin interfered with many of the commonly used procedures for the identification and quantitative estimation of the by-products of metabolic activity.

The investigation is in progress and will be reported in detail in a subsequent paper.

[1] The work described in this report was done under a contract, recommended by the Committee on Medical Research, between the office of Scientific Research and Development and the University of Chicago.

[2] The streptomycin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for experimental investigations recommended by the Committee on Chemotherapeutics and Other Agents, National Research Council.

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IN THE LABORATORY

The Assay of New Rich Natural Sources of Ascorbic Acid

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Plant materials which are reported as containing very high concentrations of ascorbic acid include the hips of wild Alberta roses, *Rosa* sp. (1,300–3,500 mg./100 grams of flesh) (*5*); hips of a cultivated rose, *Rosa laxa* (3,000–5,000 mg./100 grams of flesh) (*5, 6*); green English walnuts, *Juglans regia* (2,000–3,000 mg./100 grams) (*8*); a gooseberry found in India and West China, *Phyllanthus Emblica* (920 mg./100 ml. juice) (*2*); and recently there has been reported the finding of 1,000–3,300 mg. of ascorbic acid/100 grams of edible matter in the West Indian cherry, *Malpighia punicifolia* (*1*).

It is well recognized that there exist in some fresh plant materials, notably green walnuts, certain non-vitamin C substances that reduce the dye, 2:6-dichlorophenolindophenol, on titration with which most published values for ascorbic acid in food materials depend. Means for differentiating true vitamin C from such non-vitamin C reductants are also well established (*3, 4, 9*).

We have shown, in the case of rose hips that non-vitamin C reductants, if present at all, are negligible in amount and that the dye titration provides an accurate index of their true ascorbic acid content (*6*). For English walnuts, which, through the kindness of J. R. van Haarlem, of the Horticultural Experiment Station, Vineland, Ontario, we had the opportunity of examining, the case is quite different, as our results in Table 1 show. The values shown for non-vitamin C reductants are based upon the method of Levy (*3*).

TABLE 1

VITAMIN C AND NON-VITAMIN C DYE REDUCTANTS IN GREEN WALNUTS (*Juglans regia*)

Tissue assayed	Weight in grams	Total dye reduction (mg. vitamin C/100 grams tissue)	True ascorbic acid (mg./100 grams tissue)	Non-vitamin C reductants (mg./100 grams tissue)	Non-vitamin C reductants (% of total dye reductants)
Whole nut.....	8.5	1,622	1,232	390	24
Whole nut.....	4.2	1,027	638	389	38
Mesocarp.....	6.1	2,114	1,830	284	13
Epicarp.....	6.7	1,312	576	736	56
Mesocarp.....	4.3	1,055	942	113	11
Mesocarp*.....	1.37	2,065	1,931	134	7
Epicarp*.....	2.13	956	578	378	39

* Tissues from the same nut.

Our assays show that the mesocarp contains more ascorbic acid than the epicarp and has a smaller proportion of non-vitamin C reductants. These findings are in accordance with the results of Wokes, *et al.* (*8*). It may also be observed that the percentage of non-vitamin C reductants varies from approximately 5 to 60 per cent of the total titration in the two tissues, and up to nearly 40 per cent in the whole green nut. The highest concentration of vitamin C in the mesocarp is nearly 2,000 mg./100 grams.

The work of Wokes, *et al.* (*7*) would suggest that the proportion of non-vitamin C reductants present in green walnuts decreases with increased maturity.

In view of such circumstances it would seem that values depending solely on the dye titration, reported for ascorbic acid in new food materials, should be accepted with much reservation.

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Autolyzed Brain Tissue as a Means of Facilitating Transmission of Experimental Poliomyelitis[1]

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Most attempts to infect various animals with poliomyelitis monkey-passage strains or infected human tissues failed until Armstrong (*1*) was able to adapt the Lansing strain from monkeys to cotton rats and from the latter to white mice. Since then many unsuccessful attempts to establish other monkey-passage strains in various rodents have been made, although the spreading factor of Duran-Reynals (*2*) and a variety of technics, such as rapid passage, brain trauma, hyperpyrexia, chilling, and use of immature animals, have been employed (*5*). Successful adaptation of a few other monkey-passage strains in cotton rats has been reported by Toomey and Takacs (*8*) and Jungeblut and Sanders (*4*).

In harvesting brains and cords from CFW (Carworth) Swiss mice paralyzed following intracerebral injection with the Lansing strain of poliomyelitis virus for the preparation of stock virus suspensions, we observed that autolyzed brain tissue removed from mice left in their cages for 7 or 8 hours after death appeared to accelerate the incubation period of

[1] Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

the disease in passage mice. The autolyzed brain tissue suspensions were bacteriologically sterile. Preliminary experiments showed that the same effect could be produced by mixing sterile, autolyzed brain tissue from normal mice with stock virus suspensions. Mice and cotton rats inoculated with autolyzed, normal brain tissue alone remained normal.

For the present studies the autolyzed brain tissues were obtained from CFW normal mice that were killed by trauma and kept at room temperature for about 16 hours. Ether should not be used for killing because it seems to interfere with autolysis. A 10 per cent suspension by weight of autolyzed brain in nutrient broth (Baltimore Biological Company, pH 6.8) was then prepared by grinding in a sterile mortar with alundum and filtered through sterile gauze. The pH of the autolyzed brain suspensions ranged from 6.9 to 7.1. The suspensions were used immediately after preparation or stored overnight in the refrigerator. All autolyzed brain tissues used were bacteriologically sterile. Adjustment of the autolyzed brain suspension to pH 4.0, using the buffer solution recommended by Hammon (*3*), did not alter its effect. The virus suspensions were prepared from the pooled brains and cords of mice paralyzed 2–5 days after inoculation in the same manner as described in a previous publication (*6*).

Combined results of 8 to 10 different experiments with Lansing poliomyelitis virus comparing the incubation period and the LD_{50} titer for CFW Swiss mice, using autolyzed brain suspension, buffered saline pH 4.0, and normal mouse serum diluents mixed with equal parts of 10 per cent virus suspension, are shown in Table 1. Groups of 8 or more mice were employed in each experiment. Control animals inoculated with autolyzed brain alone remained normal, and sections of their brains and cords were negative.

TABLE 1

Material inoculated	No. of mice	LD_{50} titer of virus	Range of incubation period (days)*	Incubation time (days) to produce 50% mortality
Lansing virus + autolyzed brain	154	1×10^{-5}	1–9	3
Lansing virus + buffered saline pH 4.0	76	1×10^{-4}	2–18	7
Lansing virus + normal mouse serum	48	0.5×10^{-3}	3–20	8.5
Autolyzed brain control	48	0	0	0

* Number of days between inoculation and onset of paralysis.

Five hamsters were inoculated intracerebrally (0.05 cc.) with 10 per cent Lansing strain in autolyzed brain diluent. Two became paralyzed after 24 hours, a third on the 2nd day, while the remaining animals were paralyzed on the 3rd and 15th days, respectively. In each instance the virus was successfully transferred to 8 mice and was neutralized by human poliomyelitis convalescent serum known to contain protective antibodies against the Lansing strain. We failed to produce infection in hamsters inoculated repeatedly with mouse-passage Lansing strain suspended in buffered saline pH 4.0 or normal mouse serum, although successful transmission to this species has been reported previously (*7*).

Preliminary results in rhesus monkeys inoculated intracerebrally with a 10% per cent suspension of the BK, Leon, and McK[2] strains of monkey-passage virus and the Lansing mouse-passage strain suspended in autolyzed brain diluent have shown a fulminating infection with rapidly progressing flaccid paralysis and a very short incubation period. Histopathologic studies of the sections of brains and cords of these monkeys showed lesions typical of severe poliomyelitis.

Transfer of monkey-passage Leon strain to CFW Swiss mice. Ten per cent infected cord suspension from the 12th monkey-passage Leon strain[3] of poliomyelitis virus mixed with equal parts of 10 per cent autolyzed brain suspension was inoculated intracerebrally into each of 8 mice. On the 15th day one mouse developed paralysis of both front and hind legs, and the rest remained well. This animal was sacrificed, and its brain and cord suspension mixed with autolyzed brain was passaged to 8 additional mice. Two mice developed complete paralysis on the 13th and 21st day after inoculation, respectively, while the rest remained well. All of 8 mice inoculated with the third-passage virus mixed with autolyzed brain developed paralysis of one or more limbs in from 8 to 32 days. A cotton rat inoculated intracerebrally with the third-passage virus developed flaccid hind leg paralysis on the 17th day. The fourth passage was also made with autolyzed brain diluent, the 8 inoculated mice developing paralysis in from 4 to 17 days. Sections made of the brains and cords of fourth-passage mice showed lesions typical of severe poliomyelitis. The fifth passage was made with virus suspended in buffered saline pH 4.0 and inoculated intracerebrally into 8 mice, a cotton rat, and a rhesus monkey. The mice all developed paralysis in 2 to 9 days. The cotton rat showed paralysis of both fore limbs on the 8th day. The rhesus monkey had a temperature of 104.5°F. on the 5th day, paraplegia of the arms, and a right facial paralysis. On the following day this animal developed a complete quadriplegia and was sacrificed. Lesions typical of severe poliomyelitis were seen in sections of the brain and cord. Virus obtained from this monkey was passaged to a second monkey and 8 mice with positive results. The sixth-passage virus was completely neutralized by 1/100 dilution of human immune serum globulin, while control mice developed paralysis.

In cross-immunity tests mice immunized with three weekly intraperitoneal injections (0.25 cc. each) of 10 per cent active Lansing and Leon mouse-adapted strains and challenged intracerebrally on the 21st day with 10^{-2} dilution of virus were immune to the homologous strain. Lansing-immunized mice were immune to challenge with the Leon strain, but Leon-immunized mice showed no immunity to the Lansing strain.

There is always a hazard that a latent mouse neurotropic virus will be uncovered in attempting to adapt a monkey-passage strain to mice. The subsequent successful transfer to monkey of the fifth mouse passage of the Leon strain and also neutralization in high dilution with human immune serum globulin rules out the possibility of accidental contamination by a recognized spontaneous neurotropic virus in our stock mice. Furthermore, Leon-immunized mice were not immune to inoculation with Theiler's mouse encephalomyelitis virus (FA strain).

Attempts to transfer virus from other monkey-passage

[2] The BK, Leon, and McK strains were obtained through the courtesy of Dr. John F. Kessel.

[3] Isolated by Dr. John F. Kessel from human autopsy in 1937.

strains and human cases of poliomyelitis to white mice and cotton rats, using autolyzed brain diluent, are now in progress.

Summary. Autolyzed brain tissue diluent shortens the incubation period and facilitates the transfer of poliomyelitis virus to CFW Swiss mice, hamsters, and rhesus monkeys. The Leon monkey-passage strain of poliomyelitis virus was successfully adapted to CFW Swiss mice by means of this technic.

Since this manuscript was submitted we have isolated several strains of poliomyelitis virus from infected human feces and spinal cord in CFW Swiss mice by means of this technic.

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Semiquantitative Determination of Traces of Uranium: A Fluorophotometric Method for Field Use

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The method described below was devised in an attempt to meet a need for a lightweight portable apparatus for determining traces of uranium. Restrictions of portability were such as to eliminate most chemical and physical methods from consideration. The procedure adopted is an adaptation of that employed by Hernegger and Karlik (*1*) and by Hoffmann (*2*), who succeeded in determining quantities of uranium of the order of 1×10^{-4} μg.

The method used by the above-mentioned workers involves spectrophotometric measurement of the brightness of the fluorescence of a sodium fluoride bead containing traces of uranium, presumed to be in solid solution. A successful adaptation of this technique for use in a portable field kit was achieved by substituting a cast disc of more fusible material for the sodium fluoride bead and by employing a simple visual comparator. Certain features of two fluorophotometers constructed and a brief summary of the results obtained appear to be of sufficient interest to warrant publication.

The first fluorophotometer was constructed for laboratory use as follows: A General Electric AH-8 mercury lamp, powered by a constant-voltage transformer, was employed as a source of near-ultraviolet radiation. An aspheric condensing lens of optical glass was used to focus an enlarged image of the lamp on the fluorescent object. Next to the lens were placed glass filters to isolate the 365-mμ line. Corning Glass Works filters Nos. 585 and 986 were found to be satisfactory by spectrographic tests. Light of lower wave length (254 mμ) was found to excite fluorescence other than that due to the uranium-alkali-fluoride system and would also require use of optical materials other than glass. The fluorescent disc, a blank, and a reference disc of canary glass were held in a sliding carriage oriented at 45° to the axis of the illuminating system so as to permit fluorescent and reflected light to enter a Weston Photronic cell oriented at right angles to the illuminating beam. The carriage was constructed of blackened aluminum and served to mask the sometimes irregular edges of the discs. Between the carriage and the cell were placed two filters, which isolated the green fluorescence and prevented ultraviolet and blue light from entering the cell. Corning Glass Works filters Nos. 351 and 428 were employed. The output of the cell was taken through an Ayrton shunt to a sensitive galvanometer (0.001 μA/mm./M). The entire instrument, exclusive of the galvanometer and shunt, was contained in a hardwood box provided with light-tight ventilators. The integral lamp unit was lined with sheet aluminum.

TABLE 1

Relative Fluorescence of NaF-NaCl Discs* Containing Uranium

Added element	Relative fluorescence	Remarks
None	1.0	
Al	0.9	
As	0.9	Disc fragile
B	1.0	
Ba	1.0	
Be	0.9	
Bi	—	Disc fragile and discolored
Br	1.0	
Ca	1.0	
Cb	1.0 (+?)	
Cd	—	Disc adheres to platinum
Ce	0.5	Disc yellowish
Co	0.4	Disc gray
Cr	0.2	Disc pronounced yellow
Cu	0.9	Disc slightly gray
Fe	0.5	Disc yellowish
Hg	0.9	
I	1.0	
Mg	1.0	
Mn	—	Disc blue-green and adheres to Pt
Mo	1.0	
Ni	1.0	
Pb	0.3	Disc fragile and yellowish
Sb	0.3	
Si	1.0	
Sn	1.0	
Sr	1.0	
Ta	1.0	
Th	1.0	
Ti	1.0	
Tl	1.0 (+?)	
V	0.9	
W	0.9	
Zn	0.6	
Zr	1.0	

* The discs contained 35–100 μg. uranium/gram flux and, initially, a threefold excess by weight of added element. Discs were fused 10 minutes at bright red heat and weighed 1.9 grams.

This instrument was used for preliminary studies on the effect of temperature of fusion, composition, and thickness of the alkali fluoride discs, and for subsequent studies on interfering substances. It was found that a mixture of 5.75 parts

[1] Present address: Metal Hydrides, Inc., Beverly, Massachusetts.

[2] The authors wish to express their thanks to Metal Hydrides, Inc., of Beverly, Massachusetts, for financial assistance which made this work possible.

sodium fluoride with 1.00 part sodium chloride was satisfactory in all respects. The mixture fused easily at about 900° C. in a platinum crucible cover over a Bunsen or Mekker burner and, on rapid cooling in contact with a cold metal block, formed a fine-grain disc, easily separable from the platinum and sufficiently durable to withstand ordinary handling. A disc weighing 2 grams and 30 mm. in diameter was found satisfactory. The crucible covers used were shaped on a hardwood die and cleaned prior to each use by repeated fusions with the flux. The fluorescence of uranium-containing discs was increased by heating at bright red heat for 7 minutes, but decreased on more prolonged heating. Interference by several of the substances listed in Table 1 was reduced by heating, maximum fluorescence being attained in most cases in from 7 to 10 minutes.

Under the conditions cited, the fluorescence of the discs, as measured by the galvanometer deflections, showed a nearly linear relation to the uranium content over the range 0.2–50.0 μg. uranium/gram flux. At higher concentrations of uranium, up to 300 μg./gram flux, a smooth curve was obtained. (The maximum reported by Nichols and Slattery (*3*) is found at much higher concentrations.) The curves were used directly as working curves, by standardizing the instrument with a uranium glass disc at frequent intervals and making the occasional slight correction required by the blank. This type of instrument is capable of very great sensitivity, although the accuracy might be considerably improved by substitution of a phototube balanced circuit for the single barrier-layer cell.

It was required that the second fluorophotometer be portable, light, and able to withstand rough handling. Since great accuracy was not essential, an exceedingly simple type of visual comparator was used. This consisted of a comparator wheel on which were mounted standard alkali fluoride discs and a holder for the disc to be examined. The concentration of uranium in the standard discs varied geometrically from 0.1 to 200 μg./gram flux. The source of ultraviolet was a General Electric 4-watt RP-12 lamp, which may be operated from a 24-volt battery through a variable 25-ohm resistance. This lamp radiates principally in the vicinity of 365 mμ and is far more effective than the common 110-volt argon glow lamp. A Corning Glass Works filter No. 584 was used to eliminate practically all visible light. The instrument, including batteries, was housed in a specially designed plywood case measuring 6 x 7 x 10 inches (Fig. 1). The weight was only 4.8 pounds. The method of preparing discs for use in the portable comparator is similar to that mentioned above, except that, in field use, a gasoline blowtorch is used, and necessary weighings are accomplished with a portable balance. Sampling is more time consuming than the actual analysis, which requires 20 minutes at the most.

Because of the requirements imposed, standard techniques for the chemical separation of uranium from samples were not considered feasible. Under ordinary conditions, the method of Hoffmann (*2*) is satisfactory but tedious. A semi-quantitative study of the effect of relatively large amounts of impurities was undertaken and is recorded in Table 1. Of the substances studied, antimony, bismuth, cadmium, cerium, cobalt, chromium, iron, lead, manganese, and zinc were found to interfere seriously, because they quench the fluorescence due to uranium, obscure it by coloring the flux, or render the disc brittle. Northup (*4*), in a recent article, gives a more extended discussion of substances which interfere qualitatively with the fluorescence of sodium fluoride beads, together with a study of the effect of columbium, the one element which shows fluorescence similar to that due to uranium.

Several possible procedures for inactivating or volatilizing the above-mentioned impurities were tried. It might be expected that many of these elements could be volatilized as the halide by heating with ammonium chloride, hydrofluoric acid, etc. This procedure was fairly successful with iron, but in all cases significant amounts of uranium were lost. Attempts to volatilize chromium as chromyl chloride were unsuccessful for the same reason. Dilution of the sample with flux did not greatly alter the extent of interference, except that fragility was decreased.

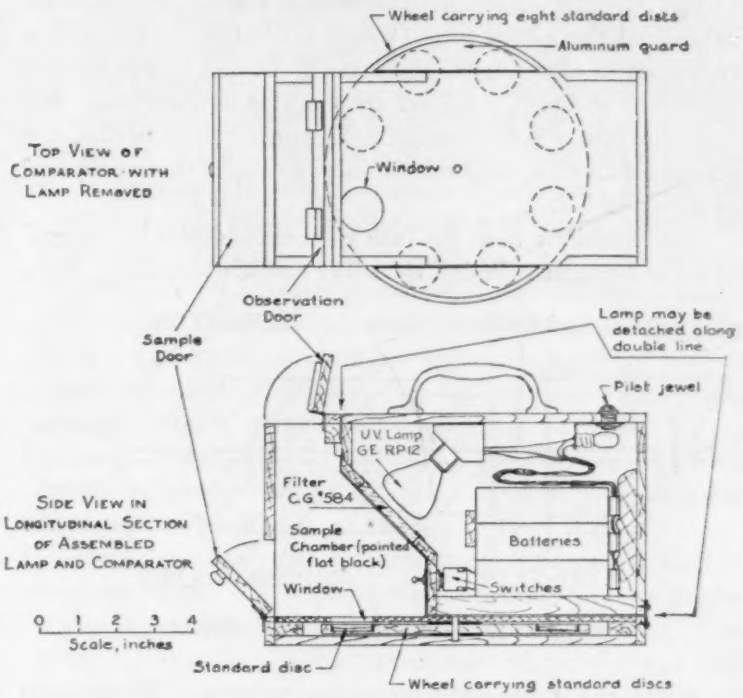

FIG. 1

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A Simple Resistance Thermometer for Blood-Temperature Measurements[1]

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In connection with an instrumentation program for the Medical Research Laboratory, Edgewood Arsenal, a compact field instrument has been developed for the intravenous meas-

[1] This work was carried out under contract with the Medical Division of the Chemical Warfare Service and was under the direction of A. H. Pfund. The authors wish to thank Capt. Lawrence Hobson (MC), AUS, for whom the instrument was constructed, for his suggestions, enthusiastic use of the instrument, and patience. We are indebted to Mr. C. B. Green, of the Bell Telephone Laboratories, for supplying the thermistor elements and pertinent information.

[2] Now with Leeds and Northrup Company, Philadelphia, Pennsylvania.

urement of animal blood temperature in the vicinity of the heart. The instrument, a resistance thermometer, is compact, easily constructed, fast responding (5 seconds), accurate, and rugged.

The Temperature-sensitive Element and Its Mounting

The temperature-sensitive element is a small, glass-coated, spheroidal thermistor bead (Western Electric V-642) with a resistance of about 1,300 ohms at 36° C. and a temperature coefficient of about −3.5 per cent at this temperature. For insertion into a vein through a 12-gauge hollow needle, the thermistor bead is mounted on the end of a 5-French catheter[3] as shown in Fig. 1.

The thermistor bead fits into a spherical recess in one end of a small copper cylinder, the other end of which is cut down

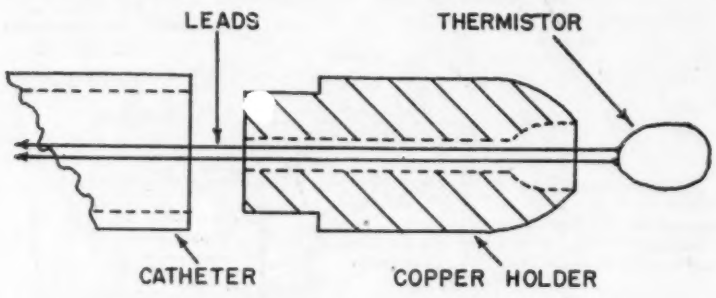

Fig. 1. Thermistor mounting details.

to match the inside diameter of the catheter. The cylinder is 0.070 inches in diameter, ¼ inch long, and has a hole (No. 72 drill) bored through its length for the thermistor leads.

Two-foot lengths of No. 32 gauge enameled copper wire are soldered to the thermistor leads, after which the soldered junctions and the thermistor leads are given a few insulating coats of thinned glyptal varnish. These leads are then threaded through the copper holder and the catheter. The copper holder is cemented into the end of the catheter with glyptal, and the bead is similarly cemented into the recess in the end of the copper. After a few hours this end of the catheter is dipped in thinned glyptal and dried in air. This is repeated until the whole assembly presents a continuous, smooth surface. Heavier copper wires are soldered to the No. 32 gauge leads at the other end of the catheter, the junctions varnished, and the wires and catheter tightly taped together. Only two leads are used because the relatively high resistance change of the element with temperature makes compensating leads unnecessary.

Associated Electrical Circuit

The circuit which translates thermistor resistance values into temperature is a conventional Wheatstone network with the thermistor in one arm. The bridge is balanced for a thermistor temperature of 46.0°, and other temperatures are read as unbalance. Since the indicating meter is a zero center meter, and the unbalance is linear for thermistor temperatures within a 10° C. range on either side of 46.0° C., the thermometer indicates temperature linearly from 36.0° C. to 56.0° C. The scale is marked off in 0.2° C. divisions and can easily be read to 0.1 ° C.

The complete electrical circuit is shown in Fig. 2. Two controls (*A*, *B*) are provided: *B* permits adjustment of the balancing resistance, and *A*, limited adjustment of the bridge potential. In order to avoid temperature errors due to heating of the element by the bridge current, a maximum of 3 volts is applied to the bridge. The bridge meter (*M*) is a Triplett Model 625 microammeter (1,000 ohms) set on the 100-0-100 microampere scale. A double throw switch allows the temperature-indicating meter to be used in standardizing the bridge voltage. The switch cuts the meter out of the bridge and puts it in series with a fixed resistance and the bridge potential. The switch has three positions (*S*, *R*, *T*). Position *S* uses the meter for bridge-voltage standardization.

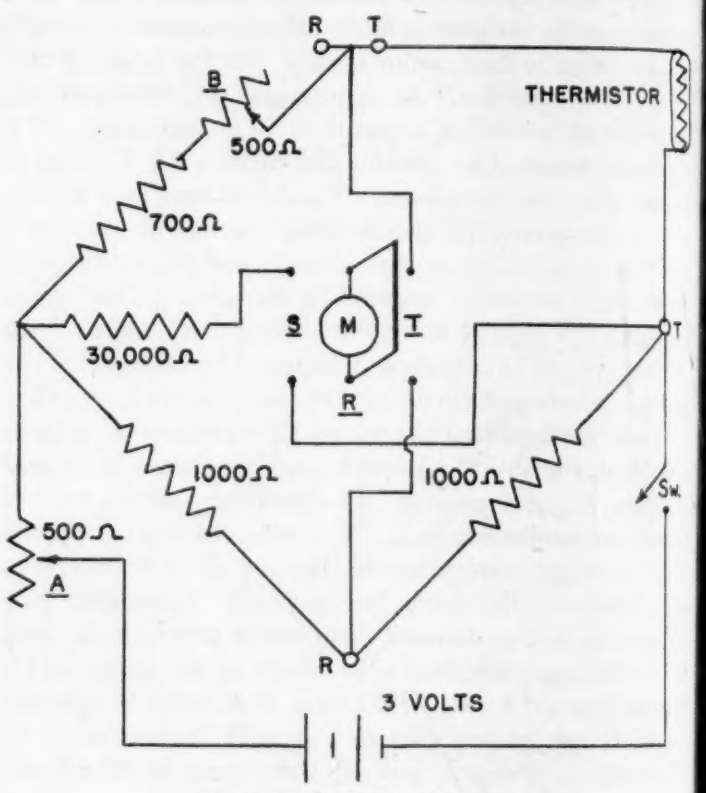

Fig. 2. Bridge circuit diagram.

With the switch in position *T*, *M* indicates the temperature of the thermistor. Position *R* disconnects the meter (*M*) from the circuit for use of auxiliary recording apparatus.

The most striking instrumental feature of the bridge is the location of all bridge elements, controls, switches, and batteries inside the case of the meter. This Triplett case measures 5½ x 6 x 2½ inches; hence, the complete bridge and meter forms a very compact unit. The zero-adjusting rheostat (*B*) and voltage-standardizing rheostat (*A*) are mounted on one side of the case, and the two switches on the other. The four terminals atop the Triplett case have been rewired as the two terminals marked T and the two marked R on the diagram. The T terminals provide bridge connections for the thermistor, and the R terminals are provided in case it is desired to use auxiliary recording equipment.

After preliminary calibration, the only check that needs to be made on the instrument before use at a later date is a voltage check, which consists of removing the thermistor, snapping the switch to position *S*, and adjusting *A* until the meter gives the standard deflection corresponding to the

[3] We have found an excellent source of very inexpensive catheters in Belden 8941 No. 20 solid lead wire with braid-lacquered insulation. The insulation is slipped off a two-foot length of wire, the loose white inside insulation is removed, and the remaining length of waterproof lacquered braid constitutes a catheter. The flexibility of the catheter is ideal for the present application.

correct bridge voltage. This deflection is determined by the preliminary calibration. After the voltage check, the thermistor is connected to the bridge, and the instrument is ready for use.

Conclusions

Several months' use of this instrument in field work under extreme conditions has proved its ruggedness and ease of handling. It has filled a definite need in the Edgewood work and should be quite useful wherever an accurate, simple, and fast thermometer is necessary in physiological studies. The introduction of another matched temperature-sensitive element in the opposite bridge arm would make this instrument applicable to the measurement of temperature differences.

The Cultivation of Mammalian Liver Cells in Large Numbers[1]

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The cultivation *in vitro* of cells of ectodermal origin may become important in certain investigations, particularly in the application of tissue culture to virus studies, biochemicar analyses, and studies of malignancy. However, the cultivation of such cells presents difficulties because of the greatel facility of growth of the connective tissue elements present in such explants.

The technic to be described was developed in the course of experiments on the attempted cultivation of the agent of infectious hepatitis. This method made it possible to produce cultures containing large numbers of liver cells with few fibroblasts, without employing a very elaborate technic. The method is based on the roller-tube technic of Gey (*2*), with the following modifications: the random distribution of many pieces of explanted tissue in roller tubes, and the use of a medium which selectively favors the growth of epithelial cells.

Materials

For a typical experiment involving 24 tubes the following sterile materials were required: 24 acid-free and grease-free test tubes, 18 x 150 mm.; a few capillary pipettes about 3 mm. in diameter at the tip; a few capillary pipettes, 200 mm. long, with the usual diameter at the tip (about 1 mm.) and bent at a 45° angle at a point 2–3 mm. from the tip; 24 solid rubber stoppers to fit the culture tubes; 3–50-cc. pointed centrifuge tubes; 1:600 heparin solution; 3–20-cc. bulb pipettes; a Petri plate, 100 mm. in diameter, containing a watch glass; a syringe and needle suitable for withdrawing 20 cc. of heart's blood from a rabbit; and a few dissecting instruments, including one fine, small, curved scissors, preferably strabismus scissors. A small amount of ice and rubber bulbs or tubing for manipulation of the pipettes are also needed.

Assembling the Culture

The explant material was obtained from a rabbit 7–10 days old, lightly anesthetized and exsanguinated. A portion of the liver was removed aseptically and placed in the watch glass contained in the Petri plate. The tissue was minced with strabismus scissors until the bits appeared to be about 1 mm. in diameter. The minced tissue was then suspended in Gey's solution (*2*) in the watch glass and transferred to a 50-cc. centrifuge tube. The top of the Petri plate was used as a shield to prevent contamination from the air. About 20 cc. of Gey's solution were then added to the tissue suspension in the tube. The latter was rotated until the tissue was distributed and was then allowed to stand. After a few minutes all the particles of about 1 mm. had settled below a well-defined plane, leaving a supernate containing erythrocytes and minute fragments. This supernate was removed by suction, and the washing of tissue fragments in Gey's solution was repeated twice more. After the supernate was removed for the third time a wide capillary pipette with rubber bulb was used to distribute small amounts of the sediment into the cotton-plugged culture tubes. The volume of the rather watery sediment which was picked up each time for placing in the culture tubes was such as to contain about 60 pieces of tissue in about 0.3 cc. of the saline solution.

The tissue was distributed by means of the capillary pipettes with bent tips. Throughout the procedure the culture tube was kept horizontal to avoid contamination from the air. The technic of distribution was as follows: The pipette was used to spread the small amount of fluid over the lower half of the tube until the entire surface was moistened, and the clump of fragments was distributed in a rough ring around the tube. Then the point of the bent tip was turned toward the surface of the tube and run up and down between the bottom of the tube and approximately halfway to the open end, while the left hand slowly rotated the tube. Bits of tissue were thus distributed over the entire lower half of the tube. Clumps remaining after this procedure were pushed apart by the tip of the capillary pipette, and any noted gross unevenness of distribution was corrected. Quite often many pairs of tissue fragments were left in contact by this procedure, but since the purpose of the method was to obtain a maximum total circumference of explants in as little time of manipulation as possible, this was not regarded as objectionable. Thus, 60 fragments which included 10 contiguous pairs would reproduce the effect of 50 entirely separate pieces. After the tissue fragments had been placed in all the tubes they were fixed in position by adding to each tube 0.25 cc. of heparinized normal rabbit plasma, which was distributed by rotating the tubes in groups of six in pipette rests until clotting was observed. After nutrient medium had been added to each tube, they were stoppered and placed in a roller-tube mechanism (*1*) rotating at 6 r.p.h.

The plasma was obtained as follows: Sterile 1:600 heparin solution (H.W.D.) was placed in a chilled tube in an ice bath, one-hundredth of the volume of blood to be drawn. Blood was then drawn from a rabbit's heart and quickly placed in the tube. Centrifugation was carried out in ice at 2,000 r.p.m. for 6 minutes, the plasma then being drawn off into another chilled centrifuge tube. This tube, if kept in ice, would not show clotting of the plasma for several hours. Within a few minutes of drawing off, however, the plasma was used to coat the tubes. The heparin concentration was such that the change of temperature from that of the ice bath to room

[1] This investigation was conducted under the Commission on Measles and Mumps, Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General, U. S. Army.

temperature was sufficient to cause clotting. It should be noted that heparinized chicken plasma, where available, may be more convenient, since it remains liquid in the refrigerator for many days and can be coagulated by the addition of hemostatic globulin.

The setting up of such a set of 24 tubes required two hours at most, from the anesthetizing of the rabbit to the placing of the tubes in the roller. This involved the work of two people and included the collection and separation of heart's blood for plasma. Bacteriologic aseptic technic was rigorously followed throughout. The rate of contamination was less than one tube per 24.

The Medium

The development of a satisfactory medium for the selective stimulation of epithelial cells was the major problem of this study. After exhaustive comparisons of salt solutions, relative amounts of serum, effect of embryonic extract, and optimum frequency of refeeding of cultures, the following medium was found to give the best results:

Balanced salt solution was made up according to Gey (*2*) except for the addition of aspartic acid, which Parshley and Sims (*3*) had found stimulating to epithelial cells of skin and thyroid when used in conjunction with Sims' salt solution. Since the addition of aspartic acid and its subsequent neutralization increased the total concentration of salt in the medium, a corresponding adjustment in the amount of NaCl was decided on by calculation. The final salt solution, identical with Gey's except for the amounts of NaOH and NaCl and the addition of aspartic acid, was made up by weighing out and dissolving (in the order shown) in double-distilled water to a final volume of 1 l. the following salts: NaCl, 8.0 grams; KCl, 0.375 gram; $CaCl_2$, 0.275 gram; $NaHCO_3$, 0.25 gram; $MgCl_2 \cdot 6\ H_2O$, 0.21 gram; Na_2HPO_4, 0.12 gram; KH_2PO_4, 0.025 gram; dextrose, 1.0 gram; and aspartic acid, 3.0 grams. Carbon dioxide was then bubbled through the solution for several minutes. NaOH was added in N/10 concentration until the pH was 7.0. The solution was sterilized by filtration through a Seitz filter. The medium as used consisted of 40 per cent of normal rabbit serum and 60 per cent of the salt solution. It was placed in the 18 x 150-mm. culture tubes in amounts of 1.6 cc. per tube, and the roller was sufficiently elevated at one end to prevent contact of the medium with the rubber stopper. Twice a week the medium was withdrawn and replaced with a similar amount of fresh medium. Once a week, between withdrawal of nutrient fluid and an addition of fresh medium, the clotting procedure was repeated in order to patch the plasma coat.

The Growth of Liver Cells

In the case of the great majority of rabbits used, the first outgrowths of liver cells from the explants could be observed in 48 hours in many fragments. In three days there were partial collars of liver cells about most of the fragments. The cells grew out radially in a rather regular form involving columns two cells wide; these would frequently curve and give off branching columns in a Y-configuration. After a few days the growth was usually such that the identity of the columns of cells was lost, and by mutual pressure the growth would form a single, continuous sheet of polygonal cells. Since the explants were often only a few millimeters apart, there was frequent contact between outgrowing sheets of cells arising from different explants. At such points of contact, growth would stop.

In more isolated explants, growth would continue until, after 10–12 days, the 1-mm. explant would be surrounded, in many cases, by collars of outgrowth 3–4 mm. wide, so that the entire sheet of cells formed an approximate circle 7–8 mm. in diameter. Thereafter, growth became markedly slower, and after the 14th day almost no extension in growth was noted. No increase in granularity of cytoplasm was observed until this time, even in the cells nearest the explant. Cultures were not maintained after the 21st day. The cells were large and polygonal, forming a continuous sheet. The nuclei were large, oval, and optically empty in the unstained preparation, with sharp borders except during mitosis. When the preparations were fixed and stained in situ, the nuclei and nucleoli were deeply stained with hematoxylin and the cytoplasm with eosin.

Not all explants, even in the best cultures, showed growth. However, so many fragments of tissue were seeded that the total area of outgrowth was considerable. Taking 3 mm. as an average of the width of the collar of outgrowth around the 1-mm. explant, we find that the sheet of liver cells from one such explant exceeded 30 mm.^{2} in area. Twenty-five such explants would provide 7 cm.^{2} of liver cells, and 33, about 10 cm.^{2} The majority of the successful tubes ranged between these two estimates. This qualification is made advisedly, because at irregular intervals either a liver would fail to grow out at all or the growth would be quite limited and short lived. For this reason, when infectious material was being studied, the cultures were originally fed with the medium described, and the infectious material was added at the time of the second feeding, after three days, at which time it was possible to predict rather accurately the course of that set of cultures. In the case of rabbits whose livers did not demonstrate good growth at that time, the infectious material was stored in the frozen state until a successful culture reached its first refeeding.

Fibroblasts were found in small numbers in almost all tubes. They occurred singly, or in small groups, between explants of liver cells. In all the tubes in which the liver cells multiplied satisfactorily the fibroblasts were very few in comparison. They were more in evidence in those in which some manipulation of the medium had interfered with the outgrowth of liver cells. In such cases there was an increase in the absolute number of those cells.

In a few tubes no fibroblasts could be found. This cannot be taken to mean that a pure culture of liver cells existed in such tubes, but the appearance of the solid sheets of liver cells, often with no other cell type in the vicinity, makes it seem possible that a pure liver culture might be derived from such explants in daughter tubes.

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Book Reviews

Electrical engineering: essential theory and typical applications. Fred H. Pumphrey. New York: Prentice-Hall, 1946. Pp. xiv + 369. (Illustrated.) $5.35.

This is a textbook in electrical engineering for students specializing in other fields. The wide range of topics treated in the volume makes it impossible for all of them to be covered in sufficient detail for the beginner, and the reader will find that many phenomena are not adequately explained. However, the bibliography at the end of each chapter is well selected and will help to solve this difficulty.

The limited material included in the chapters on direct-current machinery and circuits and alternating-current machinery and circuits is well chosen.

The relatively large space given to electron tubes and circuits is amply justified by the great importance of the electron tube as a control device in all branches of electrical engineering. The three short chapters, covering a total of 45 pages, give one of the most satisfactory introductions to the theory of electron tubes and circuits which it has been this reviewer's privilege to see.

The applications of electric energy for heating and welding and in a number of electrochemical processes are covered in a very interesting and informative manner.

In the chapter on electric motor applications the various types of loads are discussed, and the characteristics of the available motors are compared to enable the engineer to make the most satisfactory selection.

Throughout the book the drawings are particularly well made and leave no uncertainty in the mind of the reader. The photographs of details of apparatus are uniformly clear and easily understood.

This is a valuable book for the electrical engineer as well as for engineers in other branches who must make use of electricity as motive power or for control of manufacturing processes.

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Atomic and free radical reactions: the kinetics of gas-phase reactions involving atoms and organic radicals. E. W. R. Steacie. New York: Reinhold, 1946. Pp. vii + 548. $8.00.

"Information concerning elementary reactions is widely spread through the literature of chemical kinetics, photochemistry, pyrolysis, etc., and it is usually very difficult to assemble the existing data on any given reaction. This book is an attempt to bring together such data, and to treat the reactions of atoms and radicals in their own right, rather than as an incidental part of the mechanism of more complex changes." The discussion is confined to elementary reactions involving organic substances.

The book is divided into two parts. After a brief introductory chapter dealing with the elementary theory of reaction rates there are four chapters of a general character. Chapter 2 deals very fully with experimental methods (about 60 pp.). This is followed by three chapters dealing, respectively, with thermal decomposition reactions, polymerization reactions, and photochemical reactions. The material in these chapters is classified, to a large extent, according to the compound being studied. The author has given a very full account of the various proposed reaction mechanisms and has freely given his own judgment as to the extent to which the evidence should be considered conclusive in each case. This critical approach on the part of the author will make the book particularly useful to those who are not expert in this field.

The last half of the book (Chaps. 6–14) classifies reactions according to the elements, starting with carbon and hydrogen compounds, and following with chapters on compounds containing oxygen, nitrogen, chlorine, bromine, iodine, sodium, other metals, and sulfur, respectively.

Two notable features of this book are the extensive bibliography and a reaction index which includes activation energies. The latter will make this volume extremely useful in looking up all the free radical mechanisms involving a given free radical.

In the opinion of this reviewer the author is more successful in "bringing together" reactions of a given atom or radical than he is in "treating them in their own right." While it is true that Chapter 3 begins with an excellent discussion of the strength of bonds in organic molecules, little use is made of this when specific reactions are being considered.

Both the presentation of the material by the author and the format are excellent.

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Photography by infrared: its principles and applications. (2nd ed.) Walter Clark. New York: John Wiley; London: Chapman & Hall, 1946. Pp. xvii + 472. (Illustrated.) $6.00.

The pages of this book, written by Dr. Walter Clark, of the Eastman Kodak Research Laboratories, are filled with information on the general principles of photography, photography by the infrared, infrared radiation sources, value of infrared photography for various kinds of investigations, and some of the general characteristics of infrared radiation and its interaction with various materials.

The first chapter gives a general outline of the book, which is followed in the remaining 15 chapters.

In the second chapter the difference between infrared and ordinary photography is discussed. It is pointed out, with many examples, that many substances that are opaque to light are transparent to infrared radiation. Some of the necessary precautions for taking and developing pictures are then outlined, the extra care entailed by the use of infrared radiation being pointed out. There is a very complete discussion of the extension of the sensitivity of the photographic plate to longer and longer wave lengths, giving the various steps by which this has been accomplished. Plates sensitive out to 12,000 A. are now on the market. The present wave-

length limit to the sensitivity of photographic materials is at about 13,500 A. Some of the many difficulties that seem to make further progress difficult are pointed out.

There are five methods of photography in the infrared, two direct and three indirect. The first direct method is the sensitive plate; the second makes use of the Herschel effect, which is that exposure to infrared radiation destroys the effect of previous exposures to shorter wave lengths. The first indirect method depends upon the heating and vaporizing of specially prepared materials; the second makes use of the quenching of the phosphorescence of certain phosphors by infrared radiation; and the basis of the third method is the electron image tube. Probably the present-day limit to the photographic recording by infrared is at about 20,000 A.

Sources of infrared radiation, with characteristic data, are well taken care of in Chapter 7.

The next three chapters are devoted to an examination and differentiation of different materials by infrared photography. This material covers textiles, documents, art works, biological specimens, wood, coal, and botanical specimens.

Chapter 11 is devoted, with many illustrations, to infrared photomicrography. The advantages of the use of the longer wave length are many.

The special applications of this kind of photography are given, again with many illustrations. Pictures taken by the radiation from a hot electric iron are shown, as well as those of audiences taken by infrared radiation without the subjects' knowledge.

Advantage can be taken of the different properties of materials to detect camouflage by the use of infrared photography. Chapters 14, 15, and 16 are devoted to the general characteristics of infrared radiation with respect to its penetration of the atmosphere, dust, smoke, haze, and fog. The optical characteristics of materials with respect to infrared radiation differ in many instances from like characteristics for the shorter-wave-length radiation of the visible spectrum.

The book contains a very complete bibliography and index. The only criticism that can be offered is to express regret that the established nomenclature of the American Standards Association has not been followed.

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Scientific Book Register

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